```
* * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *
FILE 'HOME' ENTERED AT 14:36:28 ON 29 JAN 2003

=> file reg

=>
Uploading 10019993.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l1 full
L3          970 SEA SSS FUL L1

=> s l3 and ca/lc
      25848683 CA/LC
L4          683 L3 AND CA/LC

=> s l3 not l4
L5          287 L3 NOT L4

=> s l5 and uspatfull/lc
       4234203 USPATFULL/LC
L6            0 L5 AND USPATFULL/LC

=> s l5 and caold/lc
       1435626 CAOLD/LC
L7           12 L5 AND CAOLD/LC

=> s l5 not l7
L8          275 L5 NOT L7

=> s l8 and caplus/lc
      25935167 CAPLUS/LC
L9           10 L8 AND CAPLUS/LC

=> s l8 not l9
L10         265 L8 NOT L9

=> file ca

=> s l3
L11         253 L3

=> s cns or (central nervous)
         25349 CNS
        277272 CENTRAL
        154478 NERVOUS
         61059 CENTRAL NERVOUS
                 (CENTRAL(W)NERVOUS)
L12      75029 CNS OR (CENTRAL NERVOUS)

=> s l12 and l11
```

L13 7 L12 AND L11

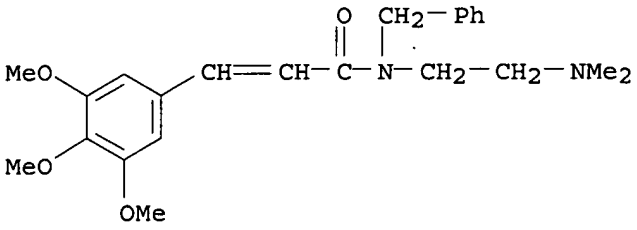
=> d ibib abs fhitstr hitrn 1-7

L13 ANSWER 1 OF 7 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:266639 CA
TITLE: The first potent and selective inhibitors of the glycine transporter type 2
AUTHOR(S): Caulfield, Wilson L.; Collie, Iain T.; Dickins, Rachel S.; Epemolu, Ola; McGuire, Ross; Hill, David R.; McVey, Gillian; Morphy, J. Richard; Rankovic, Zoran; Sundaram, Hardy
CORPORATE SOURCE: Lead Discovery Unit, Organon Laboratories Ltd., Newhouse, ML1 5SH, UK
SOURCE: Journal of Medicinal Chemistry (2001), 44(17), 2679-2682
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:266639

AB Glycine is one of the major inhibitory neurotransmitters in the spinal cord and brain stem of vertebrates. The inhibitory actions of glycine are mediated by the strychnine-sensitive glycine receptor , a ligand-gated chloride channel distributed throughout the spinal cord and brain stem. Glycine is also known to potentate the action of glutamate acting as an essential co-agonist on postsynaptic N-methyl-d- aspartate (NMDA) receptors. Synaptic levels of glycine are believed to be controlled by high-affinity glycine transporters. These transporters are members of a large family of sodium/chloride-dependent transporters, which are composed of single oligomeric proteins contg. 12 hydrophobic membrane-spanning domains. There is evidence that glycine-mediated inhibition produces muscle relaxation and blockade of this inhibition produces convulsions. Therefore, we postulated that modulators of endogenous levels of glycine might provide skeletal muscle relaxation. A significant amt. of data has accumulated over recent years, indicating that glycine also has an important role in the modulation of nociceptive pathways. Thus, it was anticipated that an increase in synaptic levels of endogenous glycine by a selective inhibition of the GlyT-2 transporter in the spinal cord may offer a unique approach for developing a novel muscle relaxant, anesthetic, and/or analgesic reagent, suitable for use during surgical anesthesia. Due to the discrete localization of both ssGlyR and the GlyT-2 transporter within the spinal cord and brain stem, a glycine modulator might not be expected to lead to serious **CNS** side effects that are characteristic for currently used .mu.-opioid analgesics. Since testing of this hypothesis has been hampered by the lack of a suitable GlyT-2 inhibitor, we sought a potent and selective inhibitor of the transporter that would enable us to conduct proof-of-principle studies. In summary, high-throughput screening of Organon's compd. collection provided an attractive drug-like GlyT-2 inhibitor suitable for high-throughput synthesis. A detailed study of the SAR and rapid hit optimization were achieved through synthesis of a soln.-phase 2D library. This led to identification of 4-benzyloxy-3,5-dimethoxy-N-[(1-di methylaminocyclopentyl)methyl]benzamide, the first potent and selective GlyT-2 inhibitor.

IT **363628-11-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity relationship of selective glycine transporter type

2 inhibitors)
RN 363628-11-9 CA
CN 2-Propenamide, N-[2-(dimethylamino)ethyl]-N-(phenylmethyl)-3-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



IT **363628-11-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity relationship of selective glycine transporter type 2 inhibitors)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 7 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:350056 CA
TITLE: Preparation of aromatic amides useful as **CNS** agents
INVENTOR(S): Bryans, Justin Stephen; O'Toole, John Colm; Horwell, David Christopher
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068184	A1	20001116	WO 2000-GB1788	20000510
W: AE, AG, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000010465	A	20020213	BR 2000-10465	20000510
EP 1178953	A1	20020213	EP 2000-927557	20000510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002544186	T2	20021224	JP 2000-617165	20000510
NO 2001005412	A	20020109	NO 2001-5412	20011106

PRIORITY APPLN. INFO.: US 1999-133359P P 19990510
WO 2000-GB1788 W 20000510

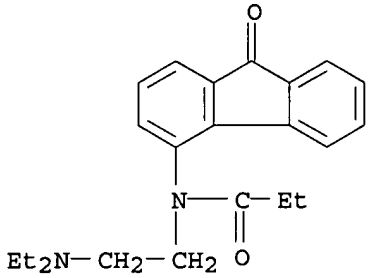
AB Arom. and heteroarom. amides R1CONR4XnNR2R3 (R1, R2, R3 = alkyl; X = alkylene; R4 = unsubstituted or substituted arom. or heteroarom. group such as naphthyl or fluorenyl), **CNS** agents useful for treating pain, depression, anxiety, seizures, and schizophrenia, were prepd. E.g.,

N-propionyl,N-(2-diethylaminoethyl)-1-amino-4-chloronaphthalene was prepd. The ability of the arom. amides to reduce the hyperalgesia effects of carrageenin was detd.

IT **305796-00-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. amides useful as **CNS** agents)

RN 305796-00-3 CA

CN Propanamide, N-[2-(diethylamino)ethyl]-N-(9-oxo-9H-fluoren-4-yl)- (9CI) (CA INDEX NAME)



IT **305796-00-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. amides useful as **CNS** agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 7 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 129:604 CA

TITLE: Substance P antagonists capable of crossing blood-brain barrier for treatment of **CNS** disease-linked diskinesia

INVENTOR(S): Imperato, Assunta; Moussaoui, Saliha; Obinu, Carmen; Gobbo, Olivier

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer S.A., Fr.; Imperato, Assunta; Moussaoui, Saliha; Obinu, Carmen; Gobbo, Olivier

SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818465	A1	19980507	WO 1997-FR1914	19971024
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2755013	A1	19980430	FR 1996-13175	19961029
FR 2755013	B1	19981127		

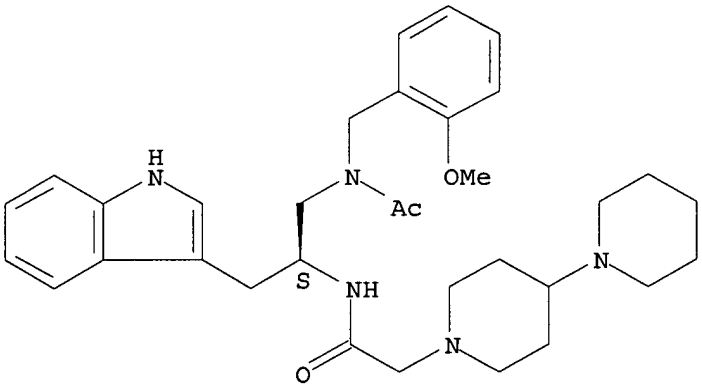
AU 9749514 A1 19980522 AU 1997-49514 19971024
PRIORITY APPLN. INFO.: FR 1996-13175 19961029
WO 1997-FR1914 19971024

AB The invention concerns the use of substance P antagonists, capable of passing through the blood-brain barrier, for prepg. a medicine for the treatment of diskinesia linked with diseases of the **central nervous** system, e.g. tardive dyskinesia.

IT **170566-85-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substance P antagonists capable of crossing blood-brain barrier for treatment of **CNS** disease-linked diskinesia)

RN 170566-85-5 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1S)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



NO

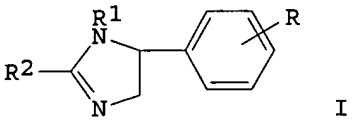
IT **170566-85-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substance P antagonists capable of crossing blood-brain barrier for treatment of **CNS** disease-linked diskinesia)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 7 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 113:172016 CA
TITLE: Preparation of 5-phenylimidazoline derivatives as **central nervous** system agents
INVENTOR(S): Tkaczynski, Tadeusz; Tkaczynska, Danuta; Kielczewska, Halina; Stefanczyk, Janusz; Kleinrok, Zdzislaw; Zebrowska-Lupina, Iwona; Stelmasiak, Malgorzata; Ossowska, Grazyna
PATENT ASSIGNEE(S): Akademia Medyczna, Lublin, Pol.
SOURCE: Pol., 4 pp.
CODEN: POXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Polish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 136249	B2	19860228	PL 1982-239765	19821223

PRIORITY APPLN. INFO.: PL 1982-239765 19821223
OTHER SOURCE(S): CASREACT 113:172016
GI

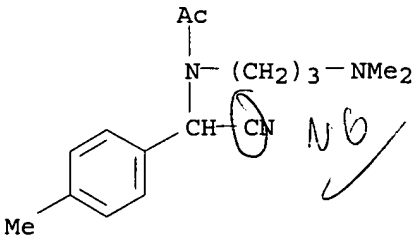


I

AB The title compds. (I; R = H, halo, alkyl, alkoxy, F3C; R1 = alkyl, aralkyl, dialkylaminoalkylene; R2 = alkyl) are prepd. by catalytic hydrogenation of the appropriate phenylacetonitrile in an org. solvent (preferably MeOH, EtOH, or PrOH) in the presence of Raney Ni at 50-180.degree.. I affect the **central nervous** system, e.g., restrict spontaneous mobility. Thus, 30 g N-acetyl-N-methyl-.alpha.-aminophenylacetonitrile in MeOH was hydrogenated over Raney Ni for 2 h at 5 MPa and 125-135.degree.. After cooling, the catalyst was sepd., MeOH was removed by distn., and the residue was vacuum distd. to give 29 g I (R = H; R1 = R2 = Me).

IT **129879-91-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(catalytic hydrogenation of)

RN 129879-91-0 CA
CN Acetamide, N-[cyano(4-methylphenyl)methyl]-N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



IT **129879-91-0 129879-92-1 129879-93-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(catalytic hydrogenation of)

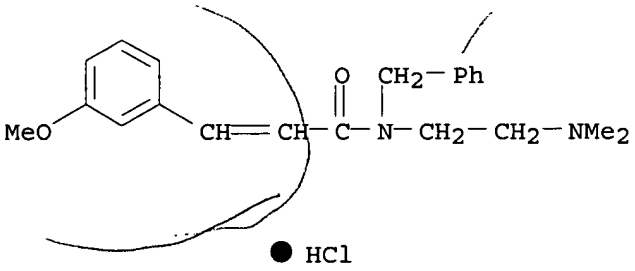
L13 ANSWER 5 OF 7 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER:	72:65203 CA
TITLE:	Alterations in brain serotonin metabolism mediating enhanced memory consolidation
AUTHOR(S):	Essman, Walter B.
CORPORATE SOURCE:	Univ. of New York, Flushing, NY, USA
SOURCE:	Present Status Psychotropic Drugs, Proc. Int. Congr. Coll. Int. Neuro-Psychopharmacol, 6th (1969), Meeting Date 1968, 305-6 CODEN: 22AKA8
DOCUMENT TYPE:	Conference
LANGUAGE:	English

AB A study was undertaken to relate pharmacol.-induced alterations in brain s erotonin (I) metabolism during learning and following a known amnesic eve nt, electroconvulsive shock (ECS), to changes in memory consolidation. Such changes were reflected in a redn. in the incidence of ECS-induced retrograde amnesia, or enhanced memory consolidation to which attendant al terations in brain I metabolism were related. Groups of male mice were injected i.p. with either 10.0 mg/kg of amitriptyline HCl (II), 10.0 mg/kg of pipradol (III), 45 mg/kg of N-[2-(dimethylamino)ethyl]-N-benzyl-3-methoxycinnamamide HCl, 1.0 mg/kg of nicotine sulfate (IV), 2.0 mg/kg of uric acid (V), or an equiv. vol. of 0.9% NaCl soln. For conditions paralleling those of drug treatment, conditioning, and ECS, mice were killed 20 min following ECS. The whole brain (excluding cerebellum and olfactory bulbs) was removed rapidly and frozen. Assays for I and 5-hydroxyindoleacetic acid (VI) were carried out. With all of the drug-treatment conditions there was a significant redn. in the incidence of ECS-induced retrograde amnesia. Brain I concn. was significantly elevated 1 hr following treatment with II (46%) and V (41%) and, under all drug treatments, VI was reduced by from 8 to 61%. When animals were trained, **central nervous** system stimulants (III, V, and IV) led to a decreased I turnover rate and increased turnover time, suggesting that I synthesis was depressed. Drug treatment, ECS or the ECS-drug interaction had no effect upon MAO activity or seizure threshold. Alterations in brain I metabolism during training, or upon administration of an amnesic event (ECS) following learning, can provide for mediation of enhanced memory consolidation.

IT **15114-65-5**
RL: BIOL (Biological study)
(serotonin metabolism response to, in brain, memory in relation to)

RN 15114-65-5 CA
CN Cinnamamide, N-benzyl-N-[2-(dimethylamino)ethyl]-m-methoxy-, monohydrochloride (8CI) (CA INDEX NAME)



NO

IT **15114-65-5**
RL: BIOL (Biological study)
(serotonin metabolism response to, in brain, memory in relation to)

L13 ANSWER 6 OF 7 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 64:75598 CA
ORIGINAL REFERENCE NO.: 64:14129c-e
TITLE: N - Acyl - N - (trialkoxyphenylalkylene)alkylenediamines
INVENTOR(S): Petracek, Francis J.
PATENT ASSIGNEE(S): Rexall Drug and Chemical Co.
SOURCE: 2 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 3234276		19660208	US	19630412

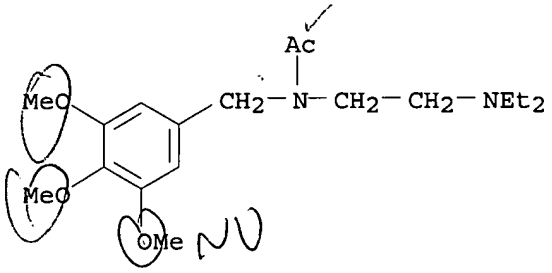
GI For diagram(s), see printed CA Issue.

AB Title compds. (I) were prepd. by treating the corresponding amine with an acid anhydride or BzCl. Thus, to 20 g. N,N-diethyl-N'-(3,4,5-trimethoxybenzyl)ethylenediamine (HCl salt m. 171-4.degree.) is added 20 g. Ac2O at 0.degree. and stirred at 0.degree. for 16 hrs. to give 81% N'-acetyl deriv. as the picrate, m. 132-5.degree.. Also prepd. was the picrate of the N-Bz deriv., m. 145.degree.. I are useful as **central nervous** system depressants.

IT **5292-94-4**, Acetamide, N-[2-(diethylamino)ethyl]-N-(3,4,5-trimethoxybenzyl)-
(prepn. of)

RN 5292-94-4 CA

CN Acetamide, N-[2-(diethylamino)ethyl]-N-(3,4,5-trimethoxybenzyl)- (7CI, 8CI) (CA INDEX NAME)



IT **5292-94-4**, Acetamide, N-[2-(diethylamino)ethyl]-N-(3,4,5-trimethoxybenzyl)- **5351-98-4**, Acetamide, N-[2-(diethylamino)ethyl]-N-(3,4,5-trimethoxybenzyl)-, picrate
(prepn. of)

L13 ANSWER 7 OF 7 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 56:67250 CA
ORIGINAL REFERENCE NO.: 56:13022a-c
TITLE: Normorphine derivatives
INVENTOR(S): Boehringer, Albert; Boehringer, Ernst; Liebrecht, Ilse; Liebrecht, Julius; Mayer-List, Walter
PATENT ASSIGNEE(S): C. H. Boehringer Sohn
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 874217		19591028	GB	
FR 1333710			FR	
US 3101339		1963	US	
PRIORITY APPLN. INFO.:			DE	19581030

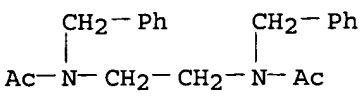
AB Quaternary derivs. of normorphine and acylnormorphines are more effective than N-allylnormorphines in antagonizing the effects of morphine. These compds. have esp. marked activity on the **central nervous** system. They are prepd. by alkylation of N-allyl- or N-propargylmorphine in an inert solvent. The following compds. are described (m.p. given): N-Diallylnormorphinium bromide, 190.degree.;N-diallylnormorphinium iodide, 164.degree.; 3,6-di-O-acetyl-N-diallylnormorphinium bromide, 188.degree.; 3,6-di-O-propionyl-N-diallylnormorphinium bromide, 190-3.degree.; N-propargyl-N-allylnormorphinium bromide, 185-6.degree., [.alpha.]20D = -99.degree. .+-. 1.degree., (c 1, MeOH); N-dipropargylnormorphinium bromide, 182.degree.; 3,6-di-O-acetyl-N-propyl-N-allylnormorphinium

bromide, c 170.degree.; N-propargyl-N-propylnormorphinium bromide, 190-3.degree.; N-dipropylnormorphinium iodide, 172-9.degree. (decompn.);N-diallylnormorphinium chloride, 179.degree.; 3,6-di-O-acetyl-N-propyl-N-propargylnormorphinium bromide, 160-5.degree. (decompn.).

IT **10507-26-3**, Acetamide, N,N'-ethylenebis[N-benzyl- (prepn. of)

RN 10507-26-3 CA

CN Acetamide, N,N'-1,2-ethanediylbis[N-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT **10507-26-3**, Acetamide, N,N'-ethylenebis[N-benzyl- (prepn. of)

=> s l11 not l13
L14 246 L11 NOT L13

=> s l14 and (pharm? or drug)
432004 PHARM?
446924 DRUG
L15 65 L14 AND (PHARM? OR DRUG)

=> d ibib abs fhitstr hitrn 1-65

L15 ANSWER 1 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 138:19472 CA
TITLE: Method of identifying inhibitors of Cdc25 using three dimensional crystal structure of the catalytic domain of Cdc25
INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark
PATENT ASSIGNEE(S): Australia
SOURCE: U.S. Pat. Appl. Publ., 246 pp., Cont.-in-part of U.S. Ser. No. 645,750.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002183249	A1	20021205	US 2001-797500	20010301
PRIORITY APPLN. INFO.:			US 1999-172215P P	19990831
			US 2000-645750 A2	20000824

OTHER SOURCE(S): MARPAT 138:19472
AB The present invention relates to the x-ray crystallog. study of proteins comprising the catalytic domains of Cdc25. The at. coordinates which result from this study are of use in identifying compds. which fit in the catalytic domain and are, therefore, potential inhibitors of Cdc25. The present invention further provides proteins which comprise the ligand

binding domain of Cdc25, cryst. forms of these proteins and the use of these cryst. forms to det. the three dimensional structure of the catalytic domain of Cdc25. The invention also relates to the use of the three dimensional structure of the Cdc25 catalytic domain in methods of designing and/or identifying potential inhibitors of Cdc25 activity, for example, compds. which inhibit the binding of a native substrate to the Cdc25 catalytic domain. These Cdc25 inhibitors are of use in methods of treating a patient having a condition which is modulated by Cdc25 activity, for example, a condition characterized by excessive, inappropriate or undesirable cellular proliferation such as cancer.

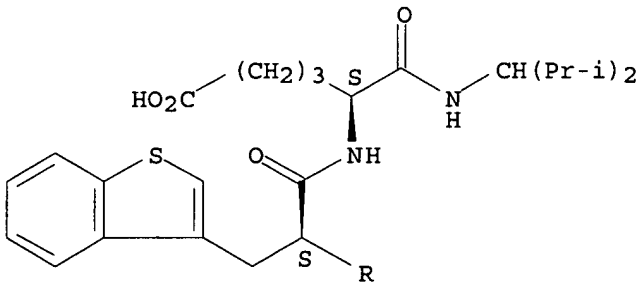
IT **329276-18-8P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of identifying inhibitors of Cdc25 using three dimensional crystal structure of catalytic domain of Cdc25)

RN 329276-18-8 CA

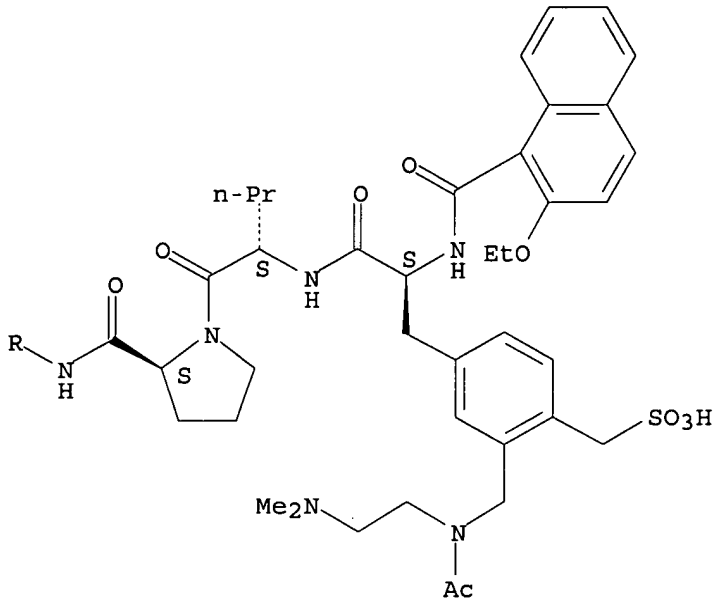
CN L-Norvalinamide, 3-[[acetyl[2-(dimethylamino)ethyl]amino]methyl]-N-[(2-ethoxy-1-naphthalenyl)carbonyl]-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-L-prolyl-3-benzo[b]thien-3-yl-L-alanyl-5-carboxy-N-[2-methyl-1-(1-methylethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT **329276-18-8P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of identifying inhibitors of Cdc25 using three dimensional crystal structure of catalytic domain of Cdc25)

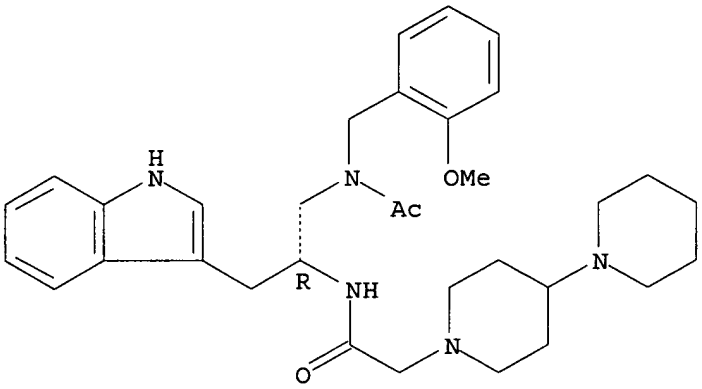
L15 ANSWER 2 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:346202 CA
TITLE: **Pharmaceutical** compositions based on anticholinergics and NK1-receptor antagonists for the treatment of respiratory tract diseases
INVENTOR(S): Pairet, Michel; Pieper, Michael P.; Meade, Christopher J. M.
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U. S. Provisional Ser. NO. 281,653.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002169181	A1	20021114	US 2002-92116	20020306
DE 10111058	A1	20020912	DE 2001-10111058	20010308
PRIORITY APPLN. INFO.:			DE 2001-10111058 A	20010308
			US 2001-281653P P	20010405

OTHER SOURCE(S): MARPAT 137:346202
AB The invention discloses **pharmaceutical** compns. based on anticholinergics and NK1-receptor antagonists, processes for prepg. them, and their use in the treatment of respiratory tract diseases. Prepn. of selected compds. is included.

IT **170566-84-4**, Lanepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticholinergics and NK1-receptor antagonists for treatment of respiratory tract diseases)
RN 170566-84-4 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4**, Lanepitant
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticholinergics and NK1-receptor antagonists for treatment of respiratory tract diseases)

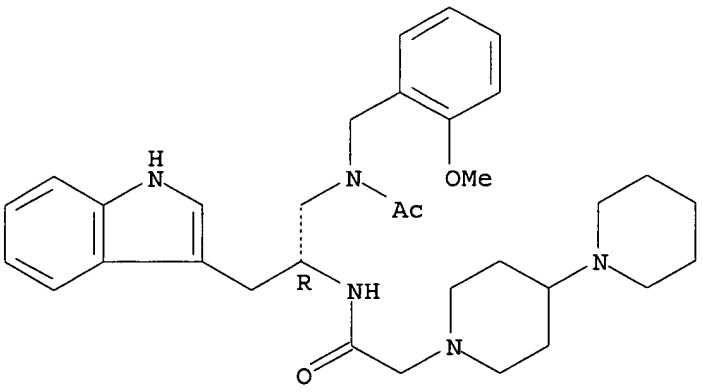
L15 ANSWER 3 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:237717 CA
TITLE: Inhalant compositions containing anticholinergics and NK1 receptor antagonists
INVENTOR(S): Meade, Christopher John Montague; Pairet, Michel; Pieper, Michael Paul
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069944	A2	20020912	WO 2002-EP1987	20020226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10111058 A1 20020912 DE 2001-10111058 20010308
PRIORITY APPLN. INFO.: DE 2001-10111058 A 20010308
OTHER SOURCE(S): MARPAT 137:237717
AB The invention relates to **drug** compns. based on anticholinergics and on NK1 receptor antagonists, to methods for their prodn., and to their use as inhalants for the treatment of respiratory tract diseases. Synthesis of NK1 receptor antagonists from the group of bis-trifluoromethyl-phenyl-piperidine derivs. are described. The products are used in suspension aerosols. Thus a compn. contained (wt./wt.%): tiotropium bromide 0.015; NK1 receptor antagonist 0.066; soy lecithin 0.2; TG11: TG12 = 2:3 to 100.
IT **170566-84-4**, Lanepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalant compns. contg. anticholinergics and NK1 receptor antagonists)
RN 170566-84-4 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4**, Lanepitant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalant compns. contg. anticholinergics and NK1 receptor antagonists)

L15 ANSWER 4 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:228607 CA
TITLE: Crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors
INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany; GPC Biotech Inc.
SOURCE: PCT Int. Appl., 351 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070680	A1	20020912	WO 2001-US6587	20010301

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2001-US6587 20010301

OTHER SOURCE(S): MARPAT 137:228607

AB Due to its role in regulating the cell cycle, Cdc25 (a family of dual specificity phosphatases) is a potential target for therapies aimed at controlling proliferative diseases, but rational, structure-based design has not been possible because of the lack of accurate 3-dimensional data. The present invention relates to polypeptides which comprises the ligand binding domain of human Cdc25 proteins, cryst. forms of these polypeptides, and the use of these cryst. forms to det. the 3-dimensional structure of the catalytic domain of Cdc25. In particular, a high resoln. crystal structure was obtained for the polypeptide denoted CDC25B(.DELTA.N8B), comprising residues Glu-368 through Arg-562 of human Cdc25B, complexed with a pentapeptide inhibitor denoted cdc1249 (2-methoxynaphthyl-1-carboxy-(4-sulfomethyl)-L-Phe-L-Glu-L-Glu-L-naphthylalanine-L-Glu-amide). The invention also relates to the use of the 3-dimensional structure of the Cdc25 catalytic domain in methods of designing and/or identifying potential inhibitors of Cdc25 activity, for example, compds. which inhibitors of Cdc25 activity, for example, compds. which inhibit the binding of a native substrate to the Cdc25 catalytic domain. The syntheses and structures of a large no. of putative pentapeptide inhibitors are also provided. Such inhibitors have potential in the treatment of diseases assocd. with excessive cellular proliferation, such as cancer, restenosis, reocclusion of coronary artery, and inflammation.

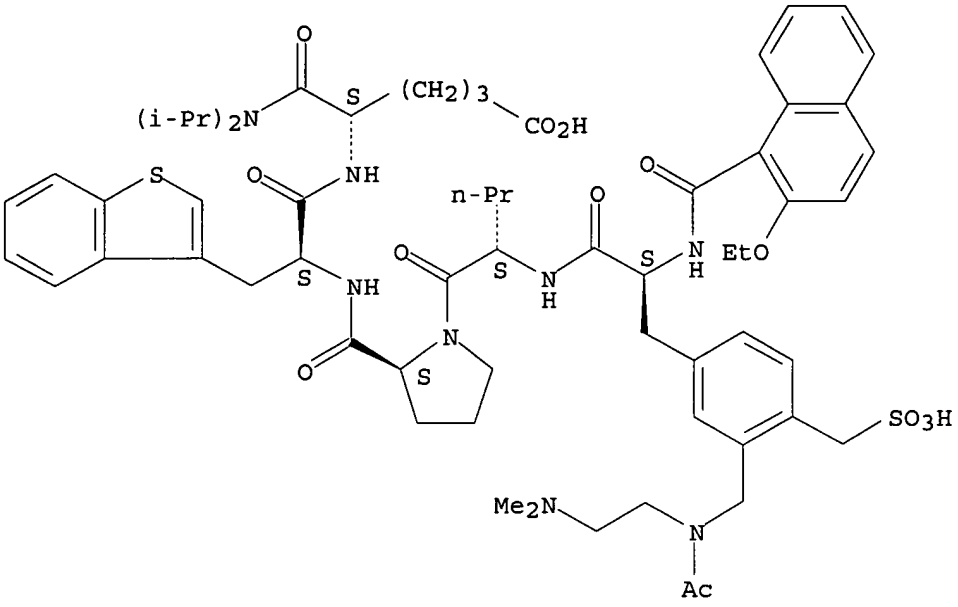
IT **457889-24-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors)

RN 457889-24-6 CA

CN L-Norvalinamide, 3-[[acetyl[2-(dimethylamino)ethyl]amino]methyl]-N-[(2-ethoxy-1-naphthalenyl)carbonyl]-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-L-prolyl-3-benzo[b]thien-3-yl-L-alanyl-5-carboxy-N,N-bis(1-methylethyl)-(9CI) (CA INDEX NAME)

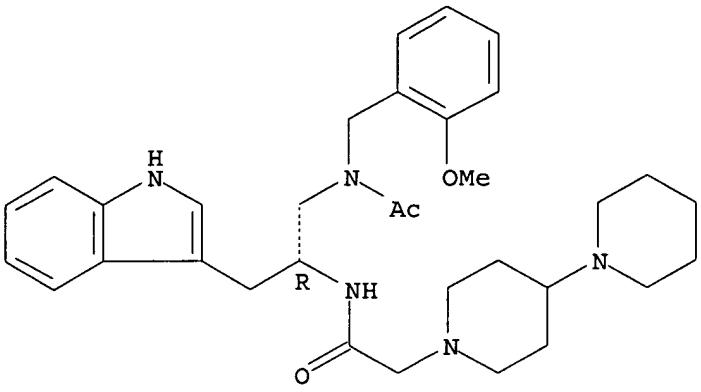
Absolute stereochemistry.



IT **457889-24-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:88400 CA
TITLE: A neural network based virtual screening of cytochrome P450 3A4 inhibitors
AUTHOR(S): Molnar, Laszlo; Keseru, Gyorgy M.
CORPORATE SOURCE: Computer Assisted Drug Discovery, Gedeon Richter Ltd., Budapest, H-1475, Hung.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(3), 419-421
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A virtual screening test to identify potential CP450 3A4 inhibitors has been developed. Mol. structures of inhibitors and non-inhibitors available in the Genetest database were represented using 2D Unity fingerprints and a feedforward neural network was trained to classify mols. regarding their inhibitory activity. Validation tests revealed that the authors neural net recognizes at least 89% of 3A4 inhibitors and suggest using this methodol. in the authors virtual screening protocol.
IT **170566-84-4**, LY303870
RL: PAC (Pharmacological activity); BIOL (Biological study)
(neural network based virtual screening of cytochrome P 450 3A4 inhibitors)
RN 170566-84-4 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

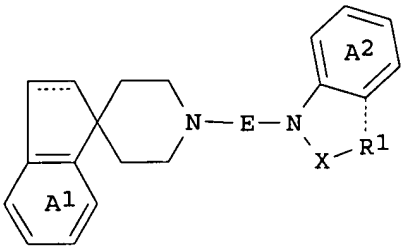


IT **170566-84-4**, LY303870
RL: PAC (Pharmacological activity); BIOL (Biological study)
(neural network based virtual screening of cytochrome P 450 3A4 inhibitors)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:294733 CA
TITLE: Preparation of spiro compounds as nociceptin receptor binders
INVENTOR(S): Arai, Toshimitsu; Nishikimi, Yuji; Imamura, Shinichi; Kamiyama, Keiji; Kobayashi, Makoto
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026714	A1	20020404	WO 2001-JP8281	20010925
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001088110	A5	20020408	AU 2001-88110	20010925
JP 2002173485	A2	20020621	JP 2001-291794	20010925

PRIORITY APPLN. INFO.: JP 2000-293876 A 20000927
WO 2001-JP8281 W 20010925
OTHER SOURCE(S): MARPAT 136:294733
GI



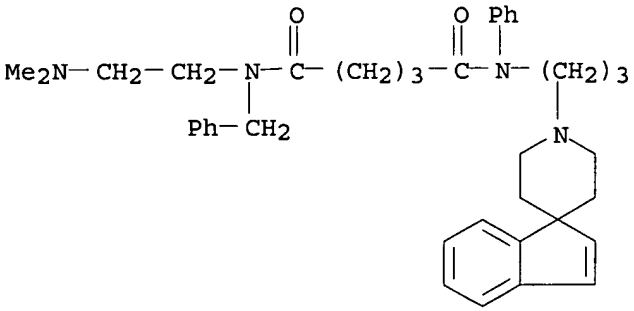
I

AB The title compds. I [A1 and A2 are each an optionally substituted benzene ring; E is a divalent chain hydrocarbon group which may be substituted; X is CO or the like; R1 is an optionally substituted hydrocarbon group or the like, or alternatively R1 may be bonded to a ring-constituting carbon atom of A2 to form a fused ring; and the dotted line represents a single or double bond; a proviso is given] are prepd. Processes for prepg. I are claimed. In an in vitro test for affinity for the nociceptin receptor, N-[3-(1H-indene-1-spiro-4'-piperidin-1'-yl)propyl]-1-methyl-5-oxo-N-phenyl-3-pyrrolidinecarboxamide fumarate at 1 .mu.M gave 95% binding inhibition. Formulations are given.

IT **407632-34-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiro compds. as nociceptin receptor binders)

RN 407632-34-2 CA

CN Pentanediamide, N-[2-(dimethylamino)ethyl]-N'-phenyl-N-(phenylmethyl)-N'-(3-spiro[1H-indene-1,4'-piperidin]-1'-ylpropyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

IT **407632-34-2P 407632-50-2P 407632-56-8P**
407632-58-0P 407632-60-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiro compds. as nociceptin receptor binders)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:54027 CA
TITLE: Preparation of vitronectin receptor antagonist **pharmaceuticals**
INVENTOR(S): Cheesman, Edward H.; Barrett, John A.; Carpenter, Alan P., Jr.; Rajopadhye, Milind; Sworin, Michael
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 318 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097861	A2	20011227	WO 2001-US20203	20010621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

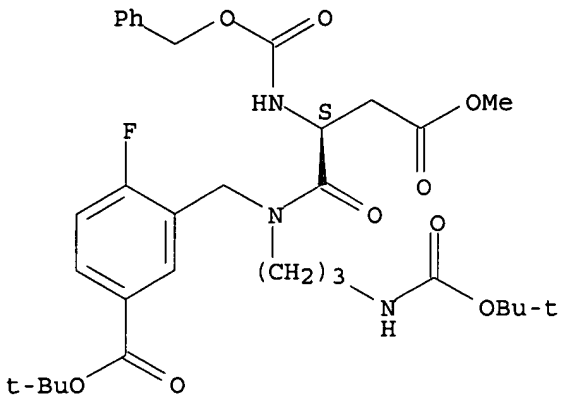
PRIORITY APPLN. INFO.: US 2000-213216P P 20000621
OTHER SOURCE(S): MARPAT 136:54027

AB The invention describes compds. (Q)d-Ln-(Ch)d' (Q is a residue having a benzodiazepine-, benzodiazepinedione-, or dibenzotrihydroannulene-type moiety , d = 1-10, d' = 1-100, Ln is a linking group, Ch is a metal-bonding unit) for use in the diagnosis and treatment of cancer in combination therapy in a patient. The present invention also provides novel compds. useful for the treatment of rheumatoid arthritis. Thus, (S,S,S)-4-[N-[3-[3,6-diaza-10-[N-(benzimidazol-2-ylmethyl)-N-methylcarbamoyl]-5-(carboxymethyl)-4-oxobicyclo[5.4.0]undeca-1(7),8,10-trien-3-yl]propyl]carbamoyl]-4-[[4-carboxy-2-[2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclodecyl]acetylamino]butanoyl]amino]butanoic acid was prepd. (claimed compd.). Syntheses of radiopharmaceticals, e.g., 99mTc(VnA)(tricine)(phosphine), where VnA represents the vitronectin receptor antagonist, are also described.

IT **277327-74-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of vitronectin receptor antagonist **pharmaceuticals**)

RN 277327-74-9 CA
CN 11-Oxa-2,5,9-triazatridecanoic acid, 5-[[5-[(1,1-dimethylethoxy)carbonyl]-2-fluorophenyl]methyl]-3-(2-methoxy-2-oxoethyl)-12,12-dimethyl-4,10-dioxo-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



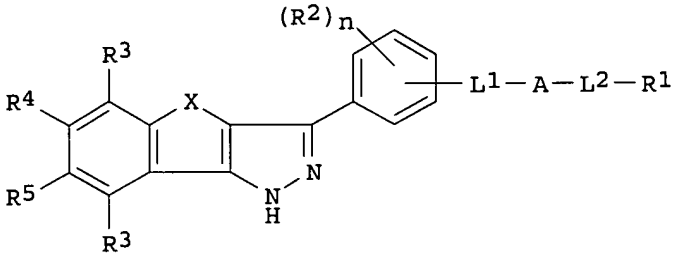
IT **277327-74-9P 277327-75-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of vitronectin receptor antagonist **pharmaceuticals**)

L15 ANSWER 8 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:272953 CA
TITLE: Substituted 1,4-dihydroindeno[1,2-c]pyrazoles as inhibitors of tyrosine kinase
INVENTOR(S): Doyle, Kevin; Rafferty, Paul; Steele, Robert; Turner, Allyson; Wilkins, David; Arnold, Lee
PATENT ASSIGNEE(S): Basf Aktiengesellschaft, Germany
SOURCE: U.S., 36 pp., Cont.-in-part of U.S. Ser. No. 541,336.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

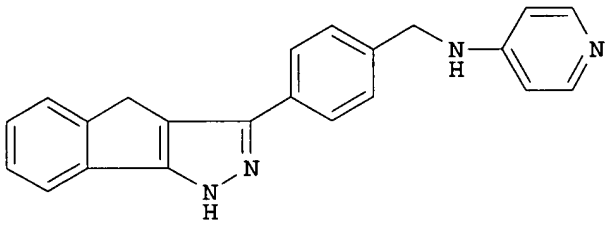
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6297238	B1	20011002	US 2000-689943	20001012
WO 2002030908	A1	20020418	WO 2001-US42715	20011012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002013485	A5	20020422	AU 2002-13485	20011012
EP 1268437	A1	20030102	EP 2001-981870	20011012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:
US 1999-127963P P 19990406
US 2000-541336 A2 20000403
US 2000-689943 A 20001012
WO 2001-US42715 W 20011012

OTHER SOURCE(S): MARPAT 135:272953
GI



I



II

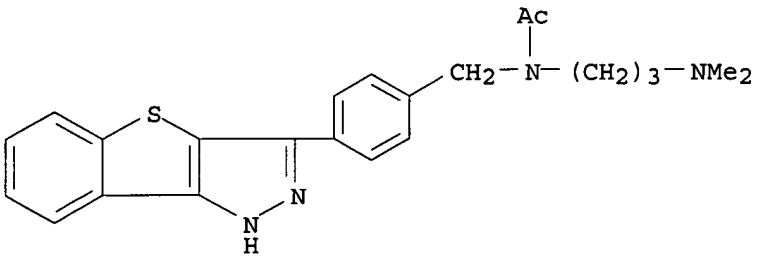
AB The title compds. I (L1 = (E)s(CH2)q {E = NRa, O or S; s = 0, 1; q = 0-6 [when s = 1, q .gtoreq. 1]; alkylene optionally (multi)substituted by: alkyl, hydroxyalkyl, OH, halo, amino deriv., (un)substituted alkoxy, etc.}; L2 = (CH2)q {optionally substituted as for L1}; A = SO2NH or NHSO2 then R1 = alkoxy, (un)substituted Ph, heteroaryl, heterocyclic nitrogen ring {which optionally contains an addnl. O, S or N atom} or amino deriv.; A = CONH or NHCO then R1 = alkoxy, substituted Ph {substituted by nitro or one or more (un)substituted alkoxy groups}, heteroaryl, heterocyclic nitrogen ring {which optionally contains an addnl. O, S or N atom}; A = NRb and q .gtoreq. 1 then R1 (un)substituted Ph, (un)substituted heteroaryl or amino deriv.; A = NRb and q = 0 then R1 = (un)substituted heteroaryl; (R2)n = (un)substituted alkyl or alkoxy, halo, OH, CN, NO2, carbamoyl, alkanoyl, alkoxycarbonyl, amino deriv. {n = 0-3}; X = substituted CH2, CO, O, C:NOR7 {R7 = H or alkyl}, NR8 {R8 = H, (un)substituted alkyl or Ph}, (CH2)n {n = 1-3}, S(O)p {p = 0-2}; R3, R4, R5 or R6 = H, halo, (un)substituted alkyl, (un)substituted alkoxy, (un)substituted phenoxy, OH, CORc {Rc = OH, alkoxy or amino deriv.}, alkanoyl, NO2, (un)substituted phenylalkyl, (un)substituted phenylalkoxy, CN, (un)substituted alkenyl or alkynyl, etc.; Ra or Rb = H, (un)substituted alkyl, alkanoyl or alkylsulfonyl) and their **pharmaceutically** acceptable salts were prepd. as inhibitors of protein kinase activity. **Pharmaceutical** compns. contg. the pyrazoles and processes for prepg. them are also disclosed. Thus, compd. II was obtained in six steps from indan-1-one with pyrazole ring formation via reaction of hydrazine hydrate with intermediate 4-(1-oxospiro[indan-2,2'-oxiran]-3'-yl)benzoic acid in the presence of glacial AcOH. All exemplified compds. significantly inhibited KDR kinase at concns. of .ltoreq. 50 .mu.M.

IT **362611-38-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted 1,4-dihydroindeno[1,2-c]pyrazoles as tyrosine kinase inhibitors)

RN 362611-38-9 CA

CN Acetamide, N-[[4-(1H-[1]benzothieno[3,2-c]pyrazol-3-yl)phenyl]methyl]-N-[3-

(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



IT **362611-38-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted 1,4-dihydroindeno[1,2-c]pyrazoles as tyrosine kinase inhibitors)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:152714 CA
TITLE: Preparation of aromatic amines and amides useful as melanocortin receptor agonists and antagonists
INVENTOR(S): Lundstedt, Torbjoern; Skottner, Anna; Seifert, Elisabeth; Andersson, Per; Kaulina, Larisa; Dikovskaya, Klara; Mutule, Ilze; Mutulis, Felikss; Wikberg, Jarl; Starchenkov, Igor; Kreicberga, Jana
PATENT ASSIGNEE(S): Melacure Therapeutics AB, Swed.; Pett, Christopher Phineas; et al.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055107	A2	20010802	WO 2001-GB356	20010129
WO 2001055107	A3	20020117		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-2056 A 20000128
GB 2000-2058 A 20000128
OTHER SOURCE(S): MARPAT 135:152714
AB The present invention relates to arom. amines and amides (I; B-E-N(R)-X-F-A and **pharmacol**. active salts thereof) and to the use of these compds. for the treatment of obesity, anorexia, inflammation, mental disorders and other diseases assocd. with the melanocortin receptors or related systems, e.g. the melanocyte stimulating hormones.

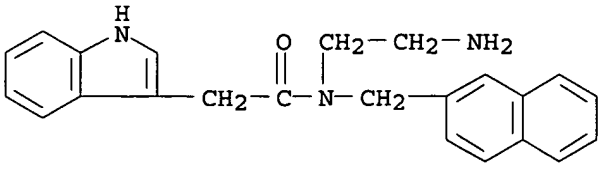
In I: X is carbonyl, methylene or is absent (i.e. it is a single bond); E and F are independently a satd. or unsatd., straight or branched chain acyclic hydrocarbon group having 1-10 C atoms, or E and/or F may be absent. R is -P-R4, -C(O)-D-R' (P and D are independently a satd. or unsatd., straight or branched chain acyclic hydrocarbon group having 1-10 C atoms; or D is absent (i.e. D is a single bond); R4 is hydroxy, cyclohexyl, cyclopentyl, guanidine, aminoguanidine, carboxy; R' is hydroxy, Me, cyclohexyl, cyclopentyl, guanidine, aminoguanidine, carboxy; or R4 or R' = (possibly substituted) amino, carbamoyl, alkoxy, alkoxycarbonyl, acyl, morpholinyl, pyrrolidinyl, piperidinyl; or R4 may be A and B as defined below). A and B are the same or different and are (possibly substituted) quinolinyl, imidazolyl, pyrazinyl, isoquinolinyl, cyclopentadienyl, pyridinyl, Ph, pyrimidinyl, pyrrolyl, isoindolyl, naphthyl, indolyl, indenyl. Several claimed compds. (N-(3-aminopropyl)-3-(1H-indol-3-yl)-N-(1,2,3,4-tetrahydronaphthalen-2-yl)propionamide, N-(5-aminopentyl)-N-(2-chloro-3-phenylallyl)-4-(1H-indol-3-yl)butyramide, [2-(1H-indol-3-yl)ethyl]bis(3-phenylpropyl)amine hydrochloride, 4-guanidino-N-[2-(1H-Indol-3-yl)ethyl]-N-(4-methoxybenzyl)butyramide hydrochloride) were tested (results given) for affinity for melanocortin receptors (MC1, MC3, MC4, MC5) and/or influence on cAMP. Anti-inflammatory effects were tested (results given) for [2-(1H-indol-3-yl)ethyl]bis(3-phenylpropyl)amine hydrochloride. Also claimed is a process for the prodn. of the claimed compds. wherein R-Y is reacted with B-E-NH-X-F-A, preferably using a std. N-alkylation procedure. Two example prepns. are given. In one example, to a soln. of 4-N-benzylbutylguanidine (10 mmol) in MeCN (15 mL) under stirring was added 1,3-bis(benzyloxycarbonyl)-2-methylthiopseudourea (10 mmol). Stirring was continued for 24 h at room temp., the reaction mixt. concd. in vacuo, purified by chromatog. (silica gel; Et acetate) to give a viscous oil (90 %). To a soln. of the above oil (N-(4-benzylaminobutyl)-N',N''-bis(benzyloxycarbonyl)guanidine) (0.5 mmol) and 3-(1H-indol-3-yl)propionic acid 2,5-dioxopyrrolidin-1-yl ester (0.5 mmol) in MeCN (10 mL) under stirring satd. NaHCO3 soln. until pH 9 was added, stirred for 2 days at room temp., evapd. in vacuo. The residue was dissolved in Et acetate (12 mL), washed with H2O (2x5 mL), dried (MgSO4) and evapd. in vacuo. To the crude intermediate dissolved in EtOH (10 mL), 5% Pd/C (20 mg) and 4 drops of concd. HCl were added and hydrogenated for 1 h at ambient pressure; the Pd catalyst was filtered off, the soln. evapd. in vacuo, and the residue purified by chromatog. (silica gel; chloroform-MeOH-H2O, 120:20:1) to give N-benzyl-N-(4-guanidinobutyl)-2-(1H-indol-3-yl)acetamide hydrochloride (47 %) as a colorless foam.

IT **352291-96-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. amines and amides useful as melanocortin receptor agonists and antagonists)

RN 352291-96-4 CA

CN 1H-Indole-3-acetamide, N-(2-aminoethyl)-N-(2-naphthalenylmethyl)- (9CI) (CA INDEX NAME)



IT **352291-96-4P 352292-00-3P 352292-06-9P**

352292-08-1P 352292-99-0P 352293-01-7P
352293-03-9P 352293-05-1P 352293-07-3P
352293-09-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. amines and amides useful as melanocortin receptor agonists and antagonists)

L15 ANSWER 10 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:152713 CA
TITLE: Aromatic amides as novel melanocortin receptor agonists and antagonists
INVENTOR(S): Lundstedt, Torbjoern; Skottner, Anna; Seifert, Elisabeth; Starchenkov, Igor; Trapencieris, Peteris; Kauss, Valerjans; Kalvins, Ivars; Boman, Arne
PATENT ASSIGNEE(S): Melacure Therapeutics AB, Swed.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055106	A2	20010802	WO 2001-GB346	20010129
WO 2001055106	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2001007893	A	20021105	BR 2001-7893	20010129
EP 1254114	A2	20021106	EP 2001-946850	20010129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: GB 2000-1948 A 20000128
GB 2000-2060 A 20000128
WO 2001-GB346 W 20010129

OTHER SOURCE(S): MARPAT 135:152713

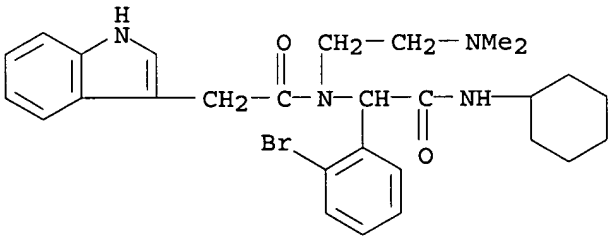
AB The present invention relates to novel arom. amides (I; B-E-X-N(R8)-C(O)-Y-F-A and **pharmacol**. active salts thereof) and to the use of these amides for the treatment of obesity, anorexia, inflammation, mental disorders and other diseases assocd. with the melanocortin receptors or related systems, e.g. the melanocyte stimulating hormones. In I: E and F are independently a satd. or unsatd., acyclic hydrocarbon group having 1-5 C atoms. X and Y are independently methylene; one of X and Y are absent (i.e. a single bond); or X can be -CH(QR10)- and/or Y can be -CH(MR9)- (M and Q are independently a satd. or unsatd., straight or branched chain acyclic hydrocarbon group with 1-6 C atoms; or M and/or Q are absent (i.e. M and/or Q are single bonds)). R8, R9 and R10 are H, -PR4, -C(O)DR4 (P and D are independently a satd. or unsatd., straight or branched chain acyclic hydrocarbon group having 1-6 C atoms; or D is absent (i.e. D is a single bond)). R4 is hydroxy, Me, cyclohexyl, cyclopentyl, aminoguanidine, guanidine, carboxy, or (possibly

substituted) amino, carbamoyl, alkoxy, alkoxycarbonyl, acyl, morpholinyl, pyrrolidinyl, piperidinyl, piperazinyl, Ph, isoindolyl, indenyl, pyridinyl, indolyl, pyrrolyl, cyclopentadienyl wherein R4 in R8, R9 and R10 may be the same or different. A and B are the same or different and are (possibly substituted) quinolinyl, isoquinolinyl, isoindolyl, naphthyl, pyridinyl, indolyl, pyrazinyl, cyclopentadienyl, pyrimidinyl, Ph, indenyl. Several claimed compds. (N-(3-aminopropyl)-3-(1H-indol-3-yl)-2-(2-naphthalen-1-ylacetylamino)propionamide hydrochloride (1:1.2), N-[1-[benzyl(4-guanidinobutyl)carbamoyl]-2-(1H-indol-3-yl)ethyl]-4-phenylbutyramide monohydrochloride, N-benzyl-N-(4-guanidinobutyl)-3-(1H-indol-3-yl)-2-(2-naphthalen-2-ylacetylamino)propionamide monohydrochloride, N-[1-(9-ethyl-9H-carbazol-3-ylcarbamoyl)-2-(1H-indol-3-yl)ethyl]-4-guanidinobutyramide monohydrochloride, 4-amino-N-[1-(9-ethyl-9H-carbazol-3-ylcarbamoyl)-2-(1H-indol-3-yl)ethyl]butyramide monohydrochloride, 2-(3-aminopropionylamino)-N-(9-ethyl-9H-carbazol-3-yl)-3-(1H-indol-3-yl)propionamide monohydrochloride) were tested (results given) for affinity for melanocortin receptors (MC1, MC3, MC4, MC5) and/or influence on cAMP. In vivo effects on food intake and anti-inflammatory effects were also detd. on selected compds. Two example prepns. are given.

IT **352277-26-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(arom. amides as novel melanocortin receptor agonists and antagonists and their prepn.)

RN 352277-26-0 CA

CN 1H-Indole-3-acetamide, N-[1-(2-bromophenyl)-2-(cyclohexylamino)-2-oxoethyl]-N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



IT **352277-26-0P 352277-28-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(arom. amides as novel melanocortin receptor agonists and antagonists and their prepn.)

L15 ANSWER 11 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER:	135:117245 CA
TITLE:	Substance P receptor antagonist and optional magnesium compound for the treatment of brain, spinal and nerve injury
INVENTOR(S):	Vink, Robert; Nimmo, Alan John
PATENT ASSIGNEE(S):	James Cook University, Australia
SOURCE:	PCT Int. Appl., 22 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052844	A1	20010726	WO 2001-AU46	20010118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001026560	A5	20010731	AU 2001-26560	20010118
BR 2001007695	A	20021015	BR 2001-7695	20010118
EP 1261335	A1	20021204	EP 2001-901048	20010118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002003423	A	20020916	NO 2002-3423	20020717

PRIORITY APPLN. INFO.: AU 2000-5146 A 20000118
WO 2001-AU46 W 20010118

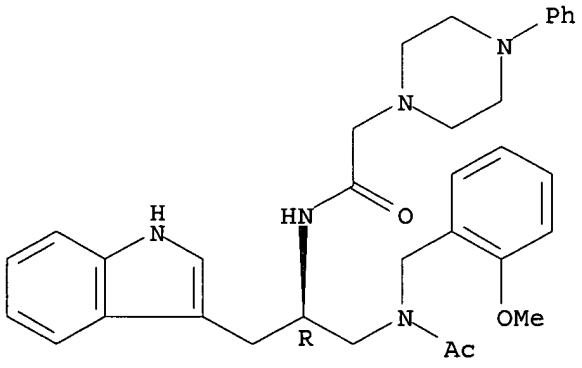
AB A treatment for brain, spinal, and nerve injury comprises use of a substance P receptor antagonist optionally in combination with a magnesium compd. Also provided is a formulation for use in the treatment comprising a substance P receptor antagonist and a magnesium compd.

IT **170566-51-5**, LY-303241
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substance P receptor antagonist and optional magnesium compd. for treatment of brain, spinal and nerve injury)

RN 170566-51-5 CA

CN 1-Piperazineacetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]-4-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-51-5**, LY-303241 **170566-84-4**, LY-303870
170567-08-5, LY-306740
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substance P receptor antagonist and optional magnesium compd. for treatment of brain, spinal and nerve injury)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:111983 CA
TITLE: NK1-Receptor antagonists for the treatment of the restless leg syndrome
INVENTOR(S): Brecht, Hans-Michael; Jung, Birgit
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 4 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

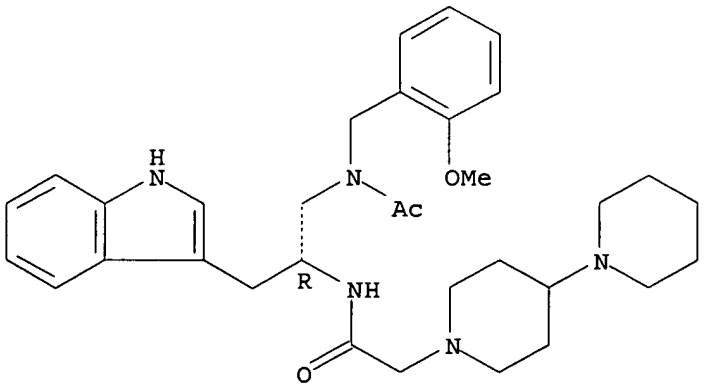
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10001785	A1	20010719	DE 2000-10001785	20000118
WO 2001052854	A1	20010726	WO 2001-EP263	20010111
W: CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2001034320	A1	20011025	US 2001-764629	20010118
PRIORITY APPLN. INFO.:			DE 2000-10001785 A	20000118
			US 2000-180399P P	20000204

AB The invention concerns the use from NK1-receptor antagonists for the prodn. of a **drug** for the treatment of the restless leg syndrome. The drugs are selected from e.g., Neuronorm, BIF 1149, FK 888, SR 48968, SR 140333, and LY 303870. Opioids, .alpha.2-adrenoceptor agonists, and Antiparkinsonian agents may be used in conjunction with NK1-receptor antagonists.

IT **170566-84-4**, LY 303870
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NK1-receptor antagonists for treatment of restless leg syndrome)

RN 170566-84-4 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4**, LY 303870
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(NK1-receptor antagonists for treatment of restless leg syndrome)

L15 ANSWER 13 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:218936 CA
TITLE: Crystal structure of CDC25 proteins and its use in rational design of inhibitors
INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark
PATENT ASSIGNEE(S): Basf Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 314 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016300	A2	20010308	WO 2000-US23473	20000825
WO 2001016300	A3	20020530		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1226237	A2	20020731	EP 2000-959449	20000825
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-172215P P 19990831
WO 2000-US23473 W 20000825

OTHER SOURCE(S): MARPAT 134:218936

AB The present invention relates to polypeptides which comprise the ligand binding domain of CDC25, cryst. forms of these polypeptides, and the use of these cryst. forms to det. the 3-dimensional structure of the catalytic domain of CDC25 alone and in complexes with pentapeptide inhibitors. At. coordinates are provided from x-ray diffraction of crystals of CDC25A and CDC25B catalytic domains in the presence and absence of various inhibitors. The invention also relates to the use of the 3-dimensional structure of the CDC25 catalytic domain in methods of designing and/or identifying potential inhibitors of CDC25 activity, for example, compds. which inhibit the binding of a native substrate to the CDC25 catalytic domain. The method comprises the steps of (1) identifying one or more functional groups capable of interacting with one or more subsites of the CDC25 catalytic domain, and (2) identifying a scaffold which presents the functional group or functional groups in a suitable orientation for interacting with one or more subsites of the CDC25 catalytic domain. Since CDC25 is a potential target for therapies aimed at controlling proliferative disease, the at. coordinates allow rational structure-based design of potential agents for the treatment of cancer, restenosis, reocclusion of coronary artery, or inflammation.

IT **329276-18-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

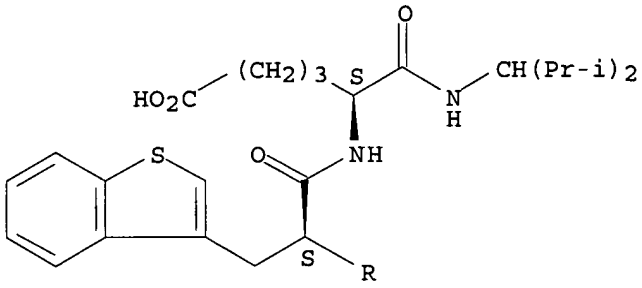
study); PREP (Preparation); USES (Uses)
(crystal structure of CDC25 proteins and its use in rational design of inhibitors)

RN 329276-18-8 CA

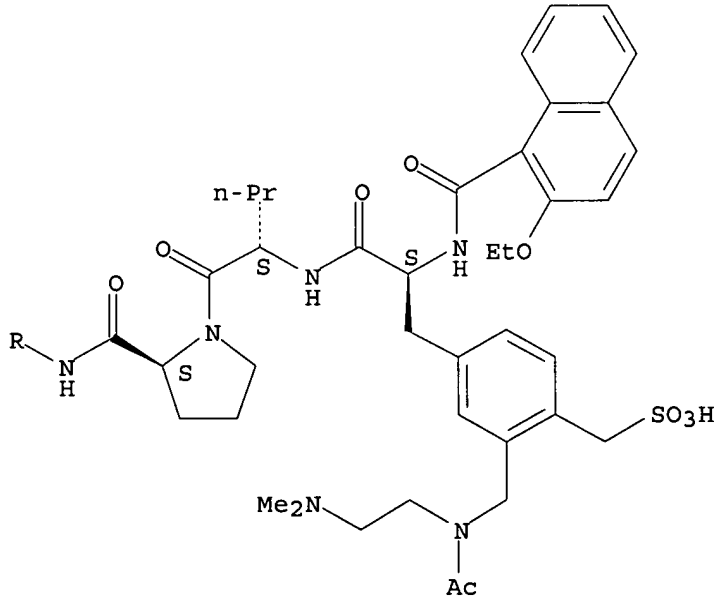
CN L-Norvalinamide, 3-[[acetyl[2-(dimethylamino)ethyl]amino]methyl]-N-[(2-ethoxy-1-naphthalenyl)carbonyl]-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-L-prolyl-3-benzo[b]thien-3-yl-L-alanyl-5-carboxy-N-[2-methyl-1-(1-methylethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT **329276-18-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure of CDC25 proteins and its use in rational design of inhibitors)

L15 ANSWER 14 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 134:168313 CA
TITLE: Targeting multimeric imaging agents through multilocus binding
INVENTOR(S): Lauffer, Randall B.; Mcmurry, Thomas J.; Dumas, Stephane; Kolodziej, Andrew; Amedio, John; Caravan, Peter; Zhang, Zhaoda; Nair, Shrikumar
PATENT ASSIGNEE(S): Epix Medical, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001008712	A2	20010208	WO 2000-US20536	20000728
WO 2001008712	A3	20020314		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013171	A	20020528	BR 2000-13171	20000728
EP 1210124	A2	20020605	EP 2000-950815	20000728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NO 2002000474	A	20020327	NO 2002-474	20020129

PRIORITY APPLN. INFO.:
US 1999-146414P P 19990729
US 1999-163650P P 19991104
WO 2000-US20536 W 20000728

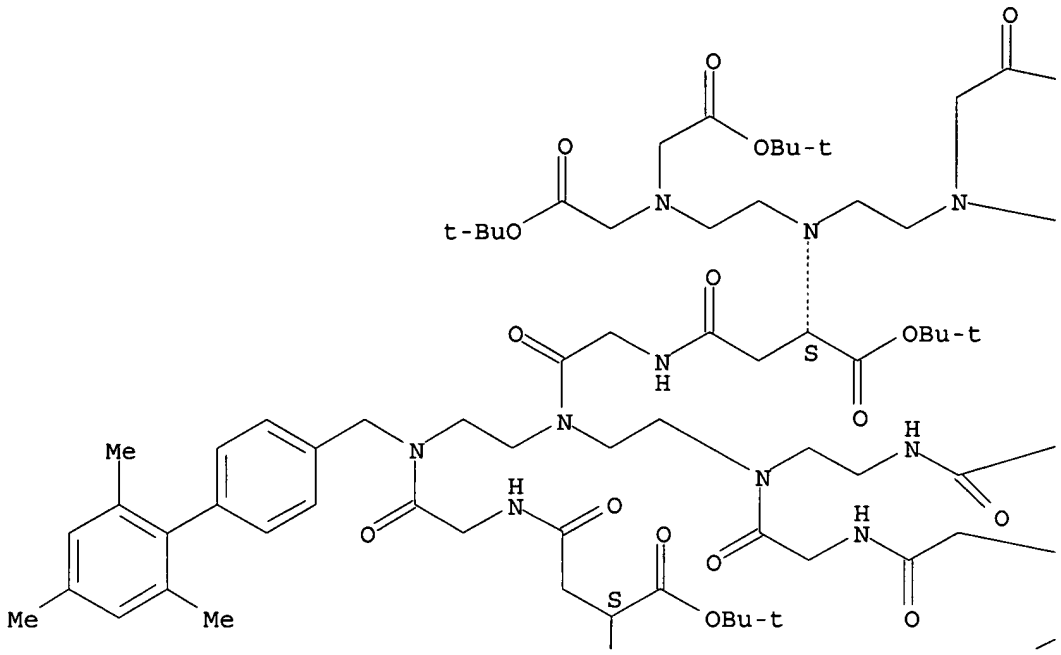
AB The present invention relates to contrast agents for diagnostic imaging. In particular, this invention relates to novel multimeric compds. which exhibit improved relaxivity properties upon binding to endogenous proteins or other physiol. relevant sites. The compds. consist of: a) two or more Image Enhancing Moieties (IEMs) (or signal-generating moiety) comprising multiple subunits; b) two or more Target Binding Moieties (TBMs), providing for in vivo localization and multimer rigidification; c) a scaffold framework for attachment of the above moieties; and d) optional linkers for attachment of the IEMs to scaffold. This invention also relates to **pharmaceutical** compns. comprising these compds. and to methods of using the compds. and compns. for contrast enhancement of diagnostic imaging.

IT **325140-34-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(targeting multimeric imaging agents through multilocus binding)

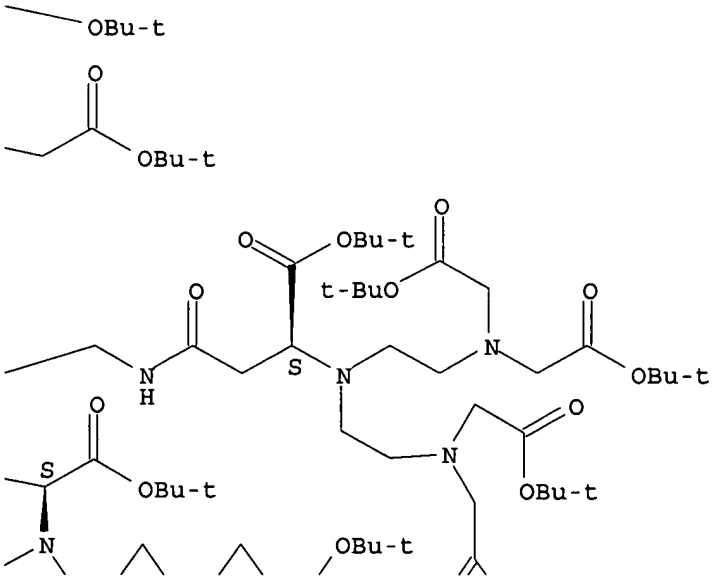
RN 325140-34-9 CA
CN Glycine, N,N-bis[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-L-.beta.-asparty1-, 1-(1,1-dimethylethyl) ester, 2,2',2'',2'''-tetraamide with N-(2-aminoethyl)-N'-[2-[[(2',4',6'-trimethyl[1,1'-biphenyl]-4-yl)methyl]amino]ethyl]-1,2-ethanediamine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

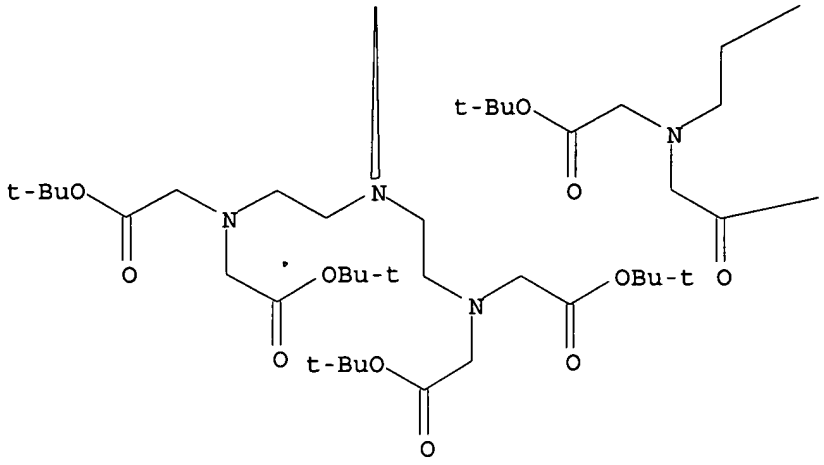
PAGE 1-A



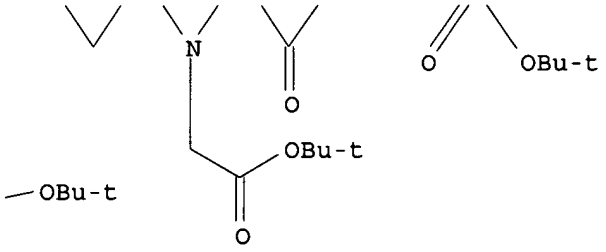
PAGE 1-B



PAGE 2-A



PAGE 2-B



IT **325140-34-9P 325140-35-0P 325140-38-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(targeting multimeric imaging agents through multilocus binding)
IT **325140-35-0DP**, gadolinium complex **325140-38-3DP**, gadolinium complex
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(targeting multimeric imaging agents through multilocus binding)

L15 ANSWER 15 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:116237 CA
TITLE: Preparation of bradykinin B1 receptor antagonists
INVENTOR(S): Ohlmeyer, Michael H. J.; Baldwin, John J.; Dolle, Roland E., III; Paradkar, Vidyadhar; Quintero, Jorge Gabriel; Pan, Gonghua
PATENT ASSIGNEE(S): Pharmacopeia, Inc., USA
SOURCE: PCT Int. Appl., 231 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001005783 A1 20010125 WO 2000-US19185 20000714
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1196411 A1 20020417 EP 2000-950343 20000714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-143990P P 19990715
WO 2000-US19185 W 20000714
OTHER SOURCE(S): MARPAT 134:116237
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

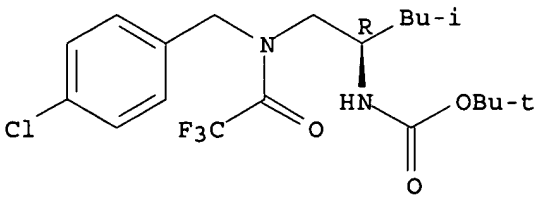
AB Compds. I [X, Y, Z = CH or N; A = A1 or A2, where A1 is R4R5NCO (R4 = H, aryl, heteroaryl, substituted alkyl; R5 = H, alkyl), 5-aryl-1,2,4-triazol-3-yl, 2-aryl-4-imidazolyl, or 2-aryl-5-thiazolyl and A2 is R7CONH (R7 = aryl or alkylaryl), R7SO2NH, R4NH, R4O; Q = heteroaryl, aryl, CH2R13 (R13 = OH, OTHP, 1-imidazolyl, 1-pyrrolyl), CH:NOMe, or 1,3-dithian-2-yl; W = H, Cl, F, alkyl, aryl, heteroaryl, alkoxy, alkylthio, an amino group, arylcarbamoyl, etc.; R1 = alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, etc.; R2 = H or alkyl or R1R2C is a ring optionally contg. O, S or N; R3 = H or alkyl, or when n is zero, R2 and R3 taken together form a 6-membered ring (with provisos)] were prepd. as bradykinin B1 receptor antagonists. Thus, D-leucine deriv. II was prepd. by substitution reaction of D-leucine 4-chlorobenzylamide with 2,4-dichloro-(or difluoro)-6-(1H-imidazol-1-yl)pyrimidine and then 3-chlorobenzylamine. **Pharmaceutical** formulations contg. II are described.

IT **321328-80-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bradykinin B1 receptor antagonists)

RN 321328-80-7 CA

CN Carbamic acid, [(1R)-1-[[[(4-chlorophenyl)methyl](trifluoroacetyl)amino]methyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **321328-80-7P 321328-82-9P 321328-84-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bradykinin B1 receptor antagonists)

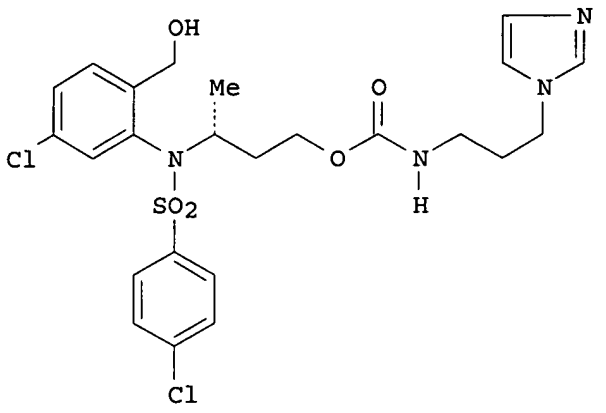
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:207678 CA
TITLE: Preparation of sulfonamide derivs. as amyloid .beta. production inhibitors useful in treating or preventing diseases related to A.beta.
INVENTOR(S): Smith, David W.; Munoz, Benito; Srinivasan, Kumar; Bergstrom, Carl P.; Chaturvedula, Prasad V.; Deshpande, Milind S.; Keavy, Daniel J.; Lau, Wai Yu; Parker, Michael F.; Sloan, Charles P.; Wallace, Owen B.; Wang, Henry Hui
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Bristol-Myers Squibb Company
SOURCE: PCT Int. Appl., 377 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050391	A1	20000831	WO 2000-US4560	20000222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1159263	A1	20011205	EP 2000-910293	20000222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008965	A	20020226	BR 2000-8965	20000222
JP 2002537376	T2	20021105	JP 2000-600975	20000222
NO 2001004135	A	20010927	NO 2001-4135	20010824

PRIORITY APPLN. INFO.:			
US 1999-121906P	P	19990226	
US 1999-122746P	P	19990226	
US 1999-122748P	P	19990226	
US 1999-130994P	P	19990423	
US 1999-130995P	A2	19990423	
WO 2000-US4560	W	20000222	

OTHER SOURCE(S): MARPAT 133:207678
GI



I

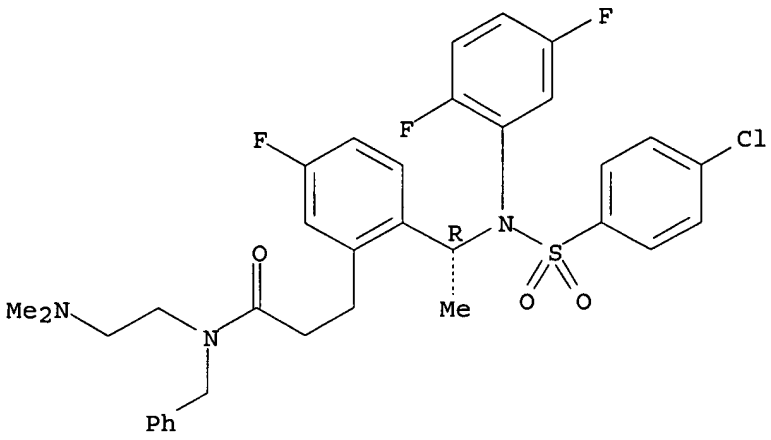
AB Title compds. [(D)(G)CHN(E)SO2(J); D = H, alkyl, heterocycle, halo, alkoxyl, ester, amide; G = alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, (CHR1)nO(CHR2)mCONR3R4, heterocycle, aryl, amine, amide, ester, ether, carbamate; D-G = cyclic; n = 1, 2, 3, 4; m = 0, 1, 2, 3, 4; R1, R2, R3, R4 are independently H, alkyl; R3-R4 = cyclic; E = H, alkyl, alkenyl, alkynyl, heterocycle, aryl, alkoxyl, amide, sulfonyl, sulfonamidyl, sulfide; J = alkyl, alkenyl, alkynyl, aryl, heterocycle, polycyclic; J-E = cyclic], **pharmaceutically** acceptable salts, and compn. comprising title compds. are prepd. Title compds. can act to modulate prodn. of amyloid .beta. protein (APP751, APP695wt, APP670/671, APP670/671/717, sAPP, .alpha.-sAPP, .beta.-sAPP) and are useful in the prevention or treatment of a variety of diseases; such diseases are amyloid angiopathy, cerebral amyloid angiopathy, systemic amyloidosis, Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis of the Dutch type, inclusion body myositis, and Down's syndrome. Thus, the title compd. I was prepd. and tested.

IT **290316-78-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonamide derivs. as amyloid .beta. prodn. inhibitors useful in treating or preventing diseases related to A.beta.)

RN 290316-78-8 CA

CN Benzenepropanamide, 2-[(1R)-1-[[(4-chlorophenyl)sulfonyl](2,5-difluorophenyl)amino]ethyl]-N-[2-(dimethylamino)ethyl]-5-fluoro-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **290316-78-8P 290320-69-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonamide derivs. as amyloid .beta. prodn. inhibitors useful in treating or preventing diseases related to A.beta.)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:202575 CA
TITLE: Identification of new Cdc25 dual specificity phosphatase inhibitors in a targeted small molecule array
AUTHOR(S): Ducruet, A. P.; Rice, R. L.; Tamura, K.; Yokokawa, F.; Yokokawa, S.; Wipf, P.; Lazo, J. S.
CORPORATE SOURCE: Combinatorial Chemistry Center and the Molecular Therapeutic/Drug Discovery Program of the University of Pittsburgh Cancer Institute, Department of Pharmacology, University of Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(6), 1451-1466
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dual specificity protein phosphatases (DSPases) are key regulators of signal transduction, oncogenesis and the cell cycle. Few potent or specific inhibitors of DSPases, however, are readily available for these **pharmacol**. targets. The authors have used a combinatorial/parallel synthetic approach to rigidify the variable core region and modify the side chains of 4-(benzyl-[2-(2,5-diphenyl-oxazole-4-carbonyl)-amino]-ethyl)-carbamoyl-2-decanoylamino butyric acid (or SC-.alpha..alpha..delta.9), which is the most active element in a previously described library of phosphatase inhibitors (Rice, R. L.; Rusnak, J. M.; Yokokawa, F.; Yokokawa, S.; Messner, D. J.; Boynton, A. L.; Wipf, P.; Lazo, J. S. Biochem. 1997, 36, 15965). Several analogs were identified as effective inhibitors of the protein tyrosine phosphatase (PTPase) PTP1B and the DSPases VHR and Cdc25B2. Two compds., FY3-.alpha..alpha.09 and FY21-.alpha..alpha.09, were partial competitive inhibitors of Cdc25B2 with Ki values of 7.6 and 1.6 .mu.M, resp.

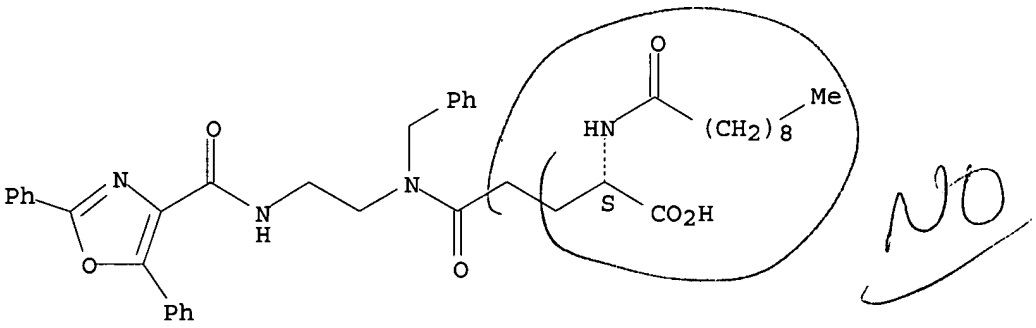
FY21-.alpha..alpha.09 possessed only moderate activity against PTP1B. Consistent with its in vitro anti-phosphatase activity, FY21-.alpha..alpha.09 inhibited growth in MDA-MB-231 and MCF-7 human breast cancer cell lines. FY21-.alpha..alpha.09 also inhibited the G2/M transition in tsFT210 cells, consistent with Cdc25B inhibition. Several architectural requirements for DSPase inhibition were revealed through modification of the side chain moieties or variable core region of the **pharmacophore**, which resulted in decreased compd. potency. The structure of FY21-.alpha..alpha.09 provides a useful platform from which addnl. potent and more highly selective phosphatase inhibitors might be generated.

IT **188403-19-2**, (S)-SC-.alpha..alpha..delta. 9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(identification of new Cdc25 dual specificity phosphatase inhibitors in a targeted small mol. array in relation to structure and lipophilicity and breast cancer inhibition and effect on cell cycle)

RN 188403-19-2 CA

CN L-Glutamine, N-[2-[[(2,5-diphenyl-4-oxazolyl)carbonyl]amino]ethyl]-N2-(1-oxodecyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



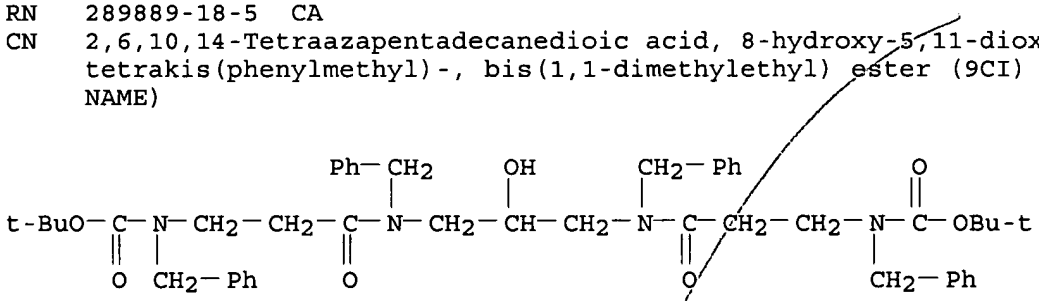
IT **188403-19-2**, (S)-SC-.alpha..alpha..delta. 9 **290330-18-6**, (R)-SC-.alpha..alpha..delta. 9 **290330-20-0**, SC-.alpha..alpha..delta. 15
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(identification of new Cdc25 dual specificity phosphatase inhibitors in a targeted small mol. array in relation to structure and lipophilicity and breast cancer inhibition and effect on cell cycle)

IT **219857-86-0P**, SC-.alpha..alpha..delta.4II **219905-92-7P**, SC-.alpha..alpha..delta.6III **290330-45-9P**, SC-.alpha..alpha..delta. 17A **290330-47-1P**, SC-.alpha..alpha..delta. 17B **290330-48-2P**, SC-.alpha..alpha..delta.A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(identification of new Cdc25 dual specificity phosphatase inhibitors in a targeted small mol. array in relation to structure and lipophilicity and breast cancer inhibition and effect on cell cycle)

IT **289906-18-9P 289906-19-0P 289906-20-3P 289906-21-4P 289906-22-5P 289906-24-7P 289906-25-8P 289906-26-9P 289906-27-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(identification of new Cdc25 dual specificity phosphatase inhibitors in

a targeted small mol. array in relation to structure and lipophilicity and breast cancer inhibition and effect on cell cycle)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 18 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:202574 CA
TITLE: New anti-HIV derivatives: synthesis and antiviral evaluation
AUTHOR(S): De Michelis, C.; Rocheblave, L.; Priem, G.; Chermann, J. C.; Kraus, J. L.
CORPORATE SOURCE: Faculte des Sciences de Luminy, Laboratoire de Chimie Biomoleculaire, Universite de la Mediterranee, Marseille, 13288, Fr.
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(6), 1253-1262
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A small focused library of 18 compds. incorporating the motif 1,3-(N,N'-dibenzyl)diamino-2-propanol has been synthesized, using adapted synthetic methodologies. These series of compds. were evaluated for their in vitro anti-HIV activity on infected MT4 cells (syncytium formation observation). Some of the new synthesized compds. show potent anti-HIV activities. EC50 values for compds. (31, 40, 34, 37 and 46) range from 0.1 to 1 .mu.M. In order to det. at which level these new derivs. interfere with the HIV replicative cycle, inhibition assays on recombinant HIV protease and HIV integrase have been performed. None of the compds. were found active on these two enzymic targets. Expts. are in progress in order to identify their biol. target within the HIV replicative cycle.
IT **289889-18-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(new anti-HIV derivs.)
RN 289889-18-5 CA
CN 2,6,10,14-Tetraazapentadecanedioic acid, 8-hydroxy-5,11-dioxo-2,6,10,14-tetrakis(phenylmethyl)-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



IT **289889-18-5P 289889-19-6P 289889-20-9P**
289889-21-0P 289889-22-1P 289889-23-2P
289889-24-3P 289889-25-4P 289889-26-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(new anti-HIV derivs.)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:99443 CA

TITLE: **Pharmacological** blockade or genetic deletion of substance P (NK1) receptors attenuates neonatal vocalization in guinea-pigs and mice

AUTHOR(S): Rupniak, N. M. J.; Carlson, E. C.; Harrison, T.; Oates, B.; Seward, E.; Owen, S.; de Felipe, C.; Hunt, S.; Wheeldon, A.

CORPORATE SOURCE: Merck Sharp and Dohme Neuroscience Research Centre, Essex, CM20 2QR, UK

SOURCE: Neuropharmacology (2000), 39(8), 1413-1421
CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

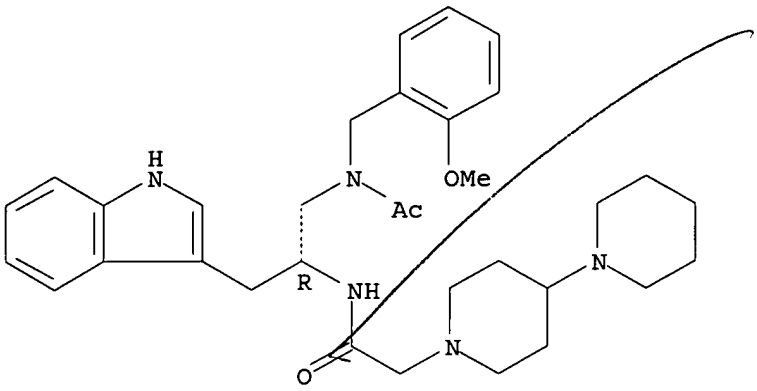
AB The regulation of stress-induced vocalizations by central NK1 receptors was investigated using **pharmacol**. antagonists in guinea-pigs, a species with human-like NK1 receptors, and transgenic NK1R-/- mice. In guinea-pigs, i.c.v. infusion of the selective substance P agonist GR73632 (0.1 nmol) elicited a pronounced vocalization response that was blocked enantioselectively by the NK1 receptor antagonists CP-99,994 and L-733,060 (0.1-10 mg/kg). GR73632-induced vocalizations were also markedly attenuated by the antidepressant drugs imipramine and fluoxetine (30 mg/kg), but not by the benzodiazepine anxiolytic diazepam (3 mg/kg) or the 5-HT1A agonist buspirone (10 mg/kg). Similarly, vocalizations in guinea-pig pups sepd. from their mothers were blocked enantioselectively by the highly brain-penetrant NK1 receptor antagonists L-733,060 and GR205171 (ID50 3 mg/kg), but not by the poorly brain-penetrant compds. LY303870 and CGP49823 (30 mg/kg). Sepn.-induced vocalizations were also blocked by the anxiolytic drugs diazepam, chlordiazepoxide and buspirone (ID50 0.5-1 mg/kg), and by the antidepressant drugs phenelzine, imipramine, fluoxetine and venlafaxine (ID50 3-8 mg/kg). In normal mouse pups, GR205171 attenuated neonatal vocalizations when administered at a high dose (30 mg/kg) only, consistent with its lower affinity for the rat than the guinea-pig NK1 receptor. Ultrasound calls in NK1R-/- mouse pups were markedly reduced compared with those in WT pups, confirming the specific involvement of NK1 receptors in the regulation of vocalization. These observations suggest that centrally-acting NK1 receptor antagonists may have clin. utility in the treatment of a range of anxiety and mood disorders.

IT **170566-84-4**, LY303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substance P (NK1) receptor **pharmacol**. blockade or genetic deletion attenuates neonatal stress-induced vocalization in guinea-pigs and mice in relation to NK1 antagonist role in treating anxiety and mood disorders)

RN 170566-84-4 CA

CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4**, LY303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substance P (NK1) receptor **pharmacol**. blockade or genetic deletion attenuates neonatal stress-induced vocalization in guinea-pigs and mice in relation to NK1 antagonist role in treating anxiety and mood disorders)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 20 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:59101 CA
TITLE: Preparation of vitronectin receptor antagonist **pharmaceuticals**
INVENTOR(S): Cheesman, Edward H.; Sworin, Michael; Rajopadhyem, Milind
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Co., USA
SOURCE: PCT Int. Appl., 228 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035887	A2	20000622	WO 1999-US30311	19991217
WO 2000035887	A3	20001116		
W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6322770	B1	20011127	US 1999-281207	19990330
US 2002015680	A1	20020207	US 1999-281209	19990330
EP 1140864	A2	20011010	EP 1999-967441	19991217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-112831P P 19981218
US 1998-80150P P 19980331
US 1998-112715P P 19981218
US 1998-112732P P 19981218

US 1998-112829P P 19981218
WO 1999-US30311 W 19991217

OTHER SOURCE(S): MARPAT 133:59101

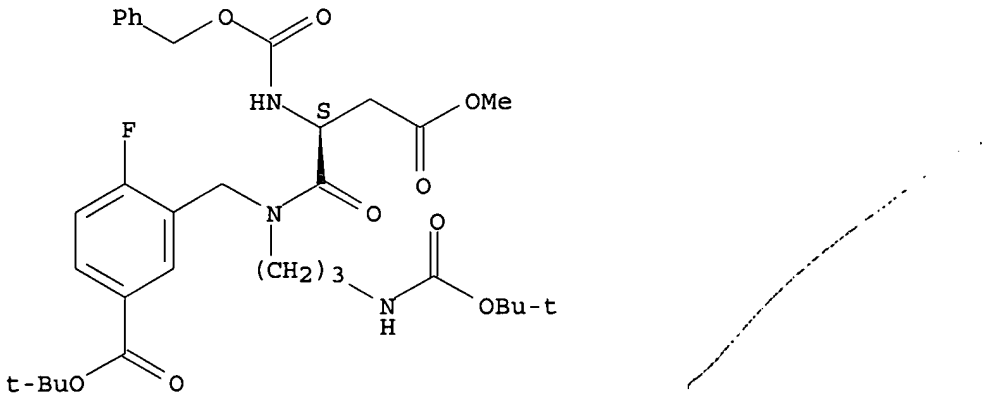
AB Compds. (Q)d-Ln-Ch (Q is a residue having a benzodiazepine-, benzodiazepinedione-, or dibenzotrihydroannulene-type moiety , d = 1-10, Ln is a linking group, Ch is a metal-bonding unit) were prepd. for use in the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compds. useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. Thus, (S,S,S)-4-[N-[3-[3,6-diaza-10-[N-(benzimidazol-2-ylmethyl)-N-methylcarbamoyl]-5-(carboxymethyl)-4-oxobicyclo[5.4.0]undeca-1(7),8,10-trien-3-yl]propyl]carbamoyl]-4-[[4-carboxy-2-[2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclodecyl]acetylamino]butanoyl]amino]butanoic acid was prepd. (claimed compd.). Syntheses of radiopharmaceticals, e.g., 99mTc(VnA)(tricine)(phosphine), where VnA represents the vitronectin receptor antagonist, are also described.

IT **277327-74-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of vitronectin receptor antagonist **pharmaceuticals**)

RN 277327-74-9 CA

CN 11-Oxa-2,5,9-triazatridecanoic acid, 5-[[5-[(1,1-dimethylethoxy)carbonyl]-2-fluorophenyl]methyl]-3-(2-methoxy-2-oxoethyl)-12,12-dimethyl-4,10-dioxo-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **277327-74-9P 277327-75-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of vitronectin receptor antagonist **pharmaceuticals**)

L15 ANSWER 21 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:342631 CA
TITLE: Lanepitant (Eli Lilly & Co)
AUTHOR(S): Ahluwalia, Amrita
CORPORATE SOURCE: Centre for Clinical Pharmacology, The Rayne Institute, London, WC1E 6JJ, UK
Current Opinion in Central & Peripheral Nervous System Investigational Drugs (2000), 2(2), 212-220
CODEN: COCDFA; ISSN: 1464-844X
PharmaPress Ltd.
Journal; General Review

LANGUAGE: English

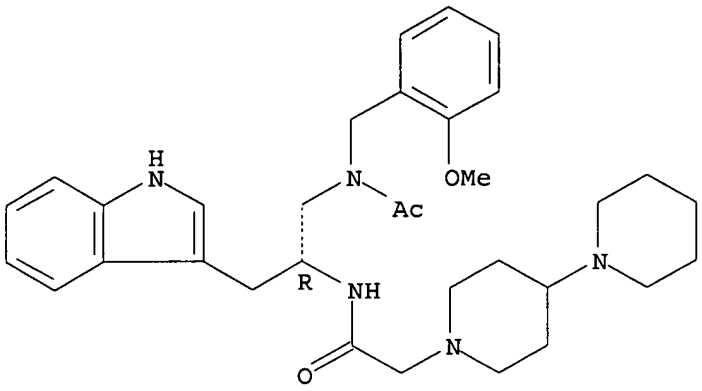
AB A review with 90 refs. Lanepitant (LY-303870) is a competitive NK1 (substance P) antagonist primarily under development by Eli Lilly as a potential treatment for migraine, for which it phase II trials have been reported. Following neg. results for phase II proof of concept trials for this indication, the current status of lanepitant is undisclosed [357864]. The compd. also has potential as a treatment for other diseases in which substance P (SP) has been implicated. These include pain, inflammation and asthma [187062]. Lilly reported results of clin. evaluations of lanepitant at the International Assocn. for the Study of Pain (Vienna, 1999). In comparison to placebo, lanepitant (200 mg) had no significant effect in preventing chronic migraine attacks over three months. Lanepitant also failed to show any significant redn. in pain scores in comparison to placebo when administered daily to patients with diabetic neuropathy. There was no detectable effect for lanepitant when administered in single doses or daily over three weeks to patients with osteoarthritis [351562]. Lilly presented results of a three-week, parallel, randomized, double-blind study in 214 outpatients with moderate to severe lower limb osteoarthritis at the 99th American Society for Clin. **Pharmacol**. and Therapeutics meeting (New Orleans, 1998). Patients were given 20, 60, 200 or 600 mg single-dose lanepitant, placebo or 375 mg naproxen, followed by 10, 30, 100 or 300 mg lanepitant, placebo or 375 mg naproxen bid. Pain intensity, pain relief, patient global impression scores and adjunctive analgesic use were compared across treatments. No statistically significant treatment differences were obsd. However, naproxen-treated patients had significantly less pain than placebo- and lanepitant-treated patients during the multiple-dose study. The study concluded that lanepitant was assocd. with diarrhea and was ineffective in relieving osteoarthritic pain [283772]. Results of a phase II study in 36 acute migraine patients were presented at the 8th Congress of the International Headache Society (June 1997, Amsterdam). This double-blind, placebo-controlled study involved 61 patients. There was no significant difference in response rate between different dosage groups (a response was defined as the conversion of a moderate-severe headache to a mild-moderate one in 2 h). The resp. response rates were 37, 22, 29 and 31% for the placebo, 30, 80 and 240 mg groups [258055]. Lanepitant was shown to be a fully functional NK1 antagonist in several in vitro assays and was orally active in a guinea pig model of inflammation. The compd. has an IC50 value of 0.15 nM [275923]. Lanepitant is claimed in WO-09514017, in which examples are presented, with affinity for the NK1 subtype in the sub-nanomolar range, and with a selectivity ratio over the NK2 subtype in the region of 1000-fold [277507].

IT **170566-84-4P**, Lanepitant
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antimigraine, analgesic, antiinflammatory and antiasthmatic testing of lanepitant)

RN 170566-84-4 CA

CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4P**, Lanepitant
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antimigraine, analgesic, antiinflammatory and antiasthmatic testing of lanepitant)

L15 ANSWER 22 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:178588 CA
TITLE: Dual G1 and G2/M phase inhibition by SC-.alpha..alpha..delta.9, a combinatorially derived Cdc25 phosphatase inhibitor
AUTHOR(S): Tamura, Kenji; Rice, Robert L.; Wipf, Peter; Lazo, John S.
CORPORATE SOURCE: Department of Pharmacology, University of Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: Oncogene (1999), 18(50), 6989-6996
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

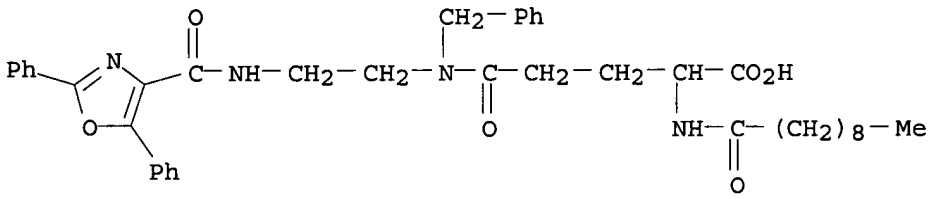
AB The Cdc25 dual specificity phosphatase family has a central role in controlling cell cycle progression and has been implicated in the etiol. of cancer. One compd., 4-(benzyl-(2-[(2,5-diphenyl-oxazole-4-carbonyl)-amino]-ethyl)-carbamoyl)-2-decanoylamino butyric acid (SC-.alpha..alpha..delta.9), was previously identified as the most potent reported synthetic inhibitor of Cdc25 phosphatases in vitro. In the present study, the authors demonstrate that SC-.alpha..alpha..delta.9 inhibited Cdc25-dependent cell cycle progression at both G1 and G2/M phase using tsFT210 cells, which express a temp.-sensitive Cdc2 mutant. SC-.alpha..alpha..delta.9 blocked both G2/M transition and dephosphorylation of Cdc2 in a concn.-dependent manner. SC-.alpha..alpha..delta.9 also enhanced tyrosine phosphorylation of both Cdk2 and Cdk4, and decreased Cdk4 kinase activity. Both of the kinases are potent regulators of G1 transition. Furthermore, closely related chem. analogs that lacked Cdc25 inhibitory activity failed to block cell cycle progression at both G1 and G2/M, and did not affect Cdc2 phosphorylation or Cdk4 kinase activity. SC-.alpha..alpha..delta.9 did not alter p53, p21 or p16 levels. The results support the hypothesis that the disruption in cell cycle transition caused by SC-.alpha..alpha..delta.9 was due to intracellular Cdc25 inhibition. The authors propose that the SC-.alpha..alpha..delta.9 **pharmacophore**

could be useful in further clarifying the role of Cdc25 phosphatase-dependent pathways in checkpoint control, oncogenesis, and apoptosis and may contribute to a further development of novel anticancer agents.

IT **219905-91-6**, SC-.alpha..alpha..delta.9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dual G1 and G2/M phase inhibition by combinatorially derived Cdc25 phosphatase inhibitor SC-.alpha..alpha..delta.9 in relation to effect on Cdc2 and and Cdk2 and Cdk4 phosphorylation and Cdk4 kinase)

RN 219905-91-6 CA

CN Glutamine, N-[2-[[(2,5-diphenyl-4-oxazolyl)carbonyl]amino]ethyl]-N2-(1-oxodecyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT **219905-91-6**, SC-.alpha..alpha..delta.9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dual G1 and G2/M phase inhibition by combinatorially derived Cdc25 phosphatase inhibitor SC-.alpha..alpha..delta.9 in relation to effect on Cdc2 and and Cdk2 and Cdk4 phosphorylation and Cdk4 kinase)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 23 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 132:146140 CA

TITLE: Three and four dimensional-quantitative structure activity relationship (3D/4D-QSAR) analyses of CYP2D6 inhibitors

AUTHOR(S): Ekins, Sean; Bravi, Gianpaolo; Binkley, Shelly; Gillespie, Jennifer S.; Ring, Barbara J.; Wikel, James H.; Wrighton, Steven A.

CORPORATE SOURCE: Departments of Drug Disposition, Lilly Research Laboratories, Eli Lilly and Co., Lilly Corporate Center, Indianapolis, IN, 46285, USA

SOURCE: Pharmacogenetics (1999), 9(4), 477-489
CODEN: PHMCEE; ISSN: 0960-314X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three- and four-dimensional quant. structure activity relationship (3D/4D-QSAR) **pharmacophore** models of competitive inhibitors of CYP2D6 were constructed using data from our lab. or the literature. The 3D-QSAR **pharmacophore** models of the common structural features of CYP2D6 inhibitors were built using the program Catalyst (Mol. Simulations, San Diego, CA, USA). These 3D-QSAR models were compared with 3D and 4D-QSAR partial least squares (PLS) models which were constructed using mol. surface-weighted holistic invariant mol. (MS-WHIM) descriptors of size and shape of inhibitors. The first Catalyst model was generated from multiple conformers of competitive inhibitors (n = 20) of CYP2D6 mediated bufurolol 1'-hydroxylation. This model demonstrated a correlation of obsd. and predicted Ki (apparent) values of r = 0.75. A

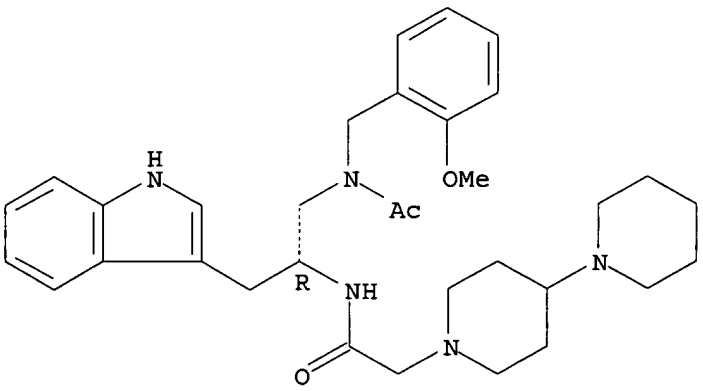
second Catalyst model was constructed from literature derived Ki (apparent) values (n = 31) for the inhibition of CYP2D6. This model provided a correlation of obsd. and predicted inhibition for CYP2D6 of r = 0.91. Both Catalyst Ki **pharmacophores** were then validated by predicting the Ki (apparent) of a test set of known CYP2D6 inhibitors (n = 15). Ten out of 15 of these Ki (apparent) values were predicted to be within one log residual of the obsd. value using our CYP2D6 inhibitor model, while the literature model predicted nine out of 15 values. Similarly, 3D- and 4D-QSARs derived from PLS MS-WHIM for our dataset yielded predictable models as assessed using cross-validation. The corresponding cross-validated PLS MS-WHIM model for the literature dataset yielded a comparable 3D-QSAR and improved 4D-QSAR value. Such computational models will aid in future prediction of **drug-drug** interactions.

IT **170566-84-4**, Ly303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3D/4D-QSAR analyses of CYP2D6 inhibitors)

RN 170566-84-4 CA

CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4**, Ly303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3D/4D-QSAR analyses of CYP2D6 inhibitors)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 24 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 131:310284 CA

TITLE: Preparation of substituted diamines as .alpha.4.beta.1 mediated cell adhesion inhibitors

INVENTOR(S): Mccarthy, Clive; Harris, Neil Victor; Morley, Andrew David

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Limited, UK

SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954321	A1	19991028	WO 1999-GB1230	19990421

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

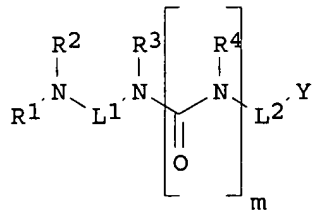
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9937164	A1	19991108	AU 1999-37164	19990421

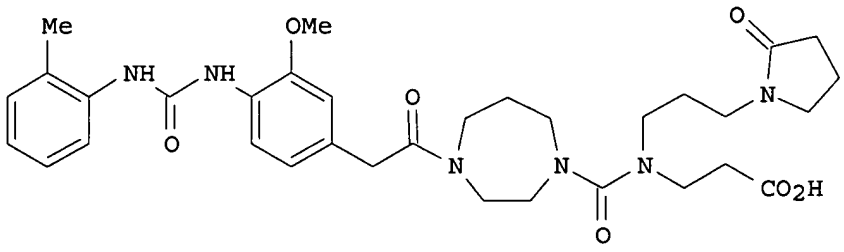
PRIORITY APPLN. INFO.:

GB 1998-8431	A	19980421
GB 1998-11417	A	19980528
US 1998-104139P	P	19981014
US 1998-104238P	P	19981014
WO 1999-GB1230	W	19990421

OTHER SOURCE(S): MARPAT 131:310284
GI



I



II

AB Substituted diamines (I) [wherein R1 = lower alkyl or various combinations of substituents, such as (cyclo)alkyl, (cyclo)alkenyl, (cyclo)alkynyl, (hetero)aryl(alkyl), etc., and linkage groups, such as C(O), C(S), (un)substituted NHC(O) or NHC(S), S(O), SO2, heteroaryldiyl, heterocycloalkylene, phenylene, etc.; R2 = H or lower alkyl; R3 and R4 = independently H or (un)substituted alkyl, alkenyl, or alkynyl; or R3 and R4 together may = (CH2)n or C(O)CH:CH; L1 = alkylene or (un)substituted (CHR10)pAr(CHR10)p; or L1N(R3) = (un)substituted alkylheterocyclo; or N(R2)L1 = (un)substituted heterocycloalkyl; or N(R2)L1N(R3) = diaza heterocyclo; L2 = (un)substituted alkylene, alkenylene, alkynylene, cycloalkenylene, cycloalkylene, or heterocycloalkylene; Y = carboxy (or an acid bioisostere) or (un)substituted C(O)NH2; Ar = phenylene, (hetero)cycloalkylene, or heteroaryldiyl; R10 = H or lower alkyl; m = 0 or

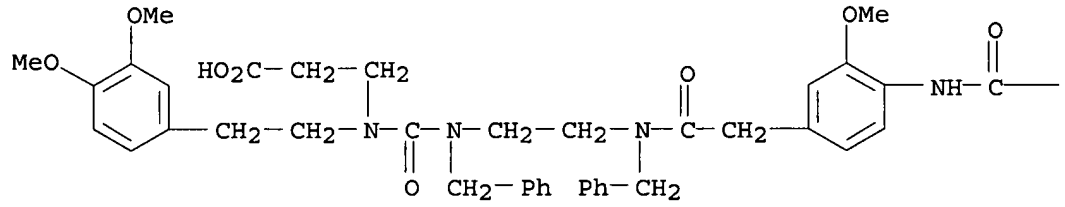
1; n = 2-4; p = 0-3] were prepd by solid phase synthesis as .alpha.4.beta.1 mediated cell adhesion inhibitors. For example, the ureido deriv. (II) was prepd. using a Wang resin support. The resin was loaded with acryloyl chloride and treated sequentially with 1-(3-aminopropyl)-2-pyrrolidinone, triphosgene, homopiperazine, and 3-methoxy-4-[3-(2-methylphenyl)ureido]phenylacetic acid to yield II. Compds. of formula I regulate the interaction of VCAM-1 and fibronectin with the integrin VLA-4 (.alpha.4.beta.1). Particular compds. of the invention suppressed cell adhesion to fibronectin and VCAM-1 with IC50 values ranging from 100.mu.M to 1 nM in assays on metabolically labeled RAMOS cells. Particular compds. also inhibited airway inflammation after antigen challenge in mice and rats. The inhibitors caused a statistically significant redn. in eosinophil and lymphocyte nos. in bronchoalveolar lavage (BAL) and airway tissue. The invention compds., their prodrugs, **pharmaceutically** acceptable salts, and solvates, are useful for the treatment of inflammatory diseases and asthma.

IT **247252-96-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of substituted diamines as .alpha.4.beta.1 mediated cell adhesion inhibitors for treatment of inflammatory diseases and asthma)

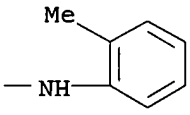
RN 247252-96-6 CA

CN .beta.-Alanine, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-[[[2-[[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl](phenylmethyl)amino]ethyl](phenylmethyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IT **247252-96-6P 247252-97-7P 247252-98-8P**
247252-99-9P 247253-00-5P 247253-01-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of substituted diamines as .alpha.4.beta.1 mediated cell adhesion inhibitors for treatment of inflammatory diseases and asthma)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 25 OF 65 CA COPYRIGHT 2003 ACS

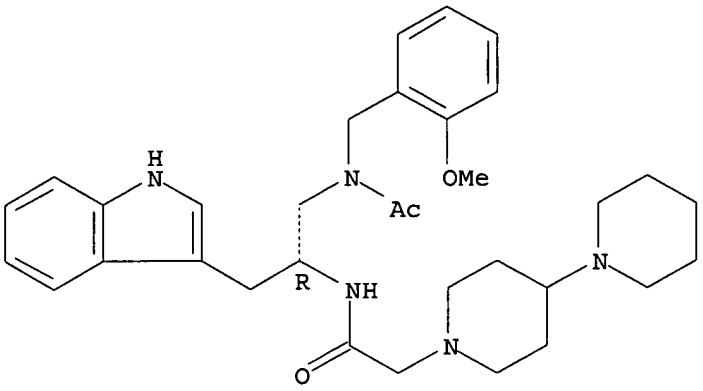
ACCESSION NUMBER: 131:208582 CA
TITLE: Three- and four-dimensional quantitative structure activity relationship analyses of cytochrome P-450 3A4 inhibitors
AUTHOR(S): Ekins, Sean; Bravi, Gianpaolo; Binkley, Shelly; Gillespie, Jennifer S.; Ring, Barbara J.; Wikel, James H.; Wrighton, Steven A.
CORPORATE SOURCE: Department of Drug Disposition, Lilly Research Laboratories, Lilly Corporate Center, Eli Lilly and Co., Indianapolis, IN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1999), 290(1), 429-438
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The program Catalyst was used to build three-dimensional quant. structure activity relationship (3D-QSAR) **pharmacophore** models of the structural features common to competitive-type inhibitors of cytochrome P 450 (CYP) 3A4. These were compared with 3D- and four-dimensional (4D)-QSAR partial least-squares (PLS) models built using mol. surface-weighted holistic invariant mol. (MS-WHIM) descriptors for size and shape of the inhibitor. The Catalyst **pharmacophore** model generated from multiple conformers of competitive inhibitors of CYP3A4-mediated midazolam 1'-hydroxylation (n = 14) yielded a high correlation of obsd. and predicted Ki values of r = 0.91. Similarly, PLS MS-WHIM was used to produce 3D- and 4D-QSARs for this data set and produced models that were statistically predictable after cross-validation. Two addnl. Catalyst **pharmacophores** were constructed from literature Ki values (n = 32) derived from the inhibition of CYP3A-mediated cyclosporin A metab. and IC50 data (n = 22) from the inhibition of CYP3A4-mediated quinine 3-hydroxylation. These Catalyst **pharmacophores** illustrated correlations of obsd. and predicted inhibition for CYP3A4 of r = 0.77 and 0.92, resp. The corresponding 4D-QSARs generated by PLS MS-WHIM for these data sets were of comparable quality as judged by cross-validation. Both Ki **pharmacophores** generated with Catalyst were also validated by predicting the Ki(apparent) values of a test set of eight CYP3A4 inhibitors not included in either model. In seven of eight cases, the residuals of the predicted Ki(apparent) values were within 1 log unit of the obsd. values. The 3D- and 4D-QSAR models produced in this study suggest the utility of future in silico prediction of CYP3A4-mediated **drug-drug** interactions.

IT **170566-84-4**, LY303870
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(3D- and 4D-QSAR analyses of cytochrome P 450 3A4 inhibitors)

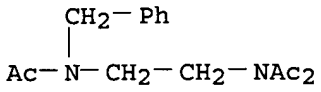
RN 170566-84-4 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



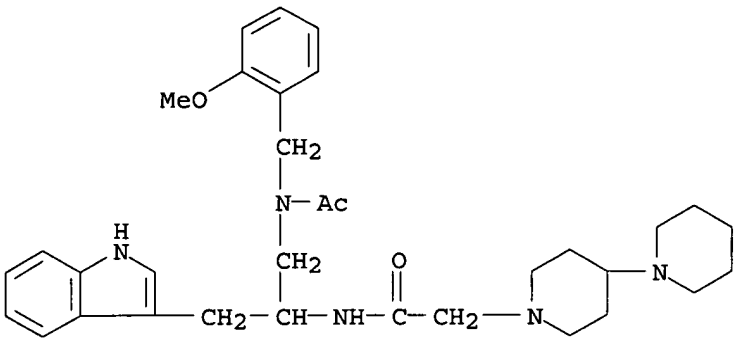
IT **170566-84-4**, LY303870
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(3D- and 4D-QSAR analyses of cytochrome P 450 3A4 inhibitors)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 26 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:181722 CA
TITLE: 99M-technetium-labelled peptide-HYNIC conjugates: Effects of lipophilicity and stability on biodistribution
AUTHOR(S): Decristoforo, Clemens; Mather, Stephen J.
CORPORATE SOURCE: Nuclear Medicine Research Laboratory, St. Bartholomew's Hospital, London, UK
SOURCE: Nuclear Medicine and Biology (1999), 26(4), 389-396
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this study was to explore the effects of lipophilicity and stability on the biodistribution of 99mTc labeled peptides through the use of different co-ligands. 6-Hydrazinopyridine-3-carboxylic acid (HYNIC) was coupled to the somatostatin analog RC160 and radiolabeled using a range of ethylenediaminediacetic acid (EDDA) and EDTA derivs. as well as tricine and pyridine/tricine as co-ligands. After labeling with technetium-99m, chromatog., stability, protein-binding, and rat biodistribution studies were performed. For most co-ligands, biodistribution correlated well with in vitro properties. Lipophilic substitution on EDDA resulted in higher protein binding, increased liver uptake, and intestinal excretion. Stabilization of tricine with pyridines reduced blood levels and lowered liver uptake. EDTA derivs. showed high instability in vitro and in vivo.
IT **103974-84-1DP**, 99mTc-labeled mixed complexes
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(effects of lipophilicity and stability on biodistribution of 99mTc-labeled peptide-HYNIC conjugates)
RN 103974-84-1 CA
CN Acetamide, N-acetyl-N-[2-[acetyl(phenylmethyl)amino]ethyl]- (9CI) (CA INDEX NAME)



IT **103974-84-1DP**, 99mTc-labeled mixed complexes
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(effects of lipophilicity and stability on biodistribution of 99mTc-labeled peptide-HYNIC conjugates)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 27 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:346558 CA
TITLE: Systematic screening approach for chiral separations of basic compounds by capillary electrophoresis with modified cyclodextrins
AUTHOR(S): Liu, Li; Nussbaum, Mark A.
CORPORATE SOURCE: Pharmaceutical Sciences Division, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1999), 19(5), 679-694
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A simple, systematic method was developed for rapidly screening potential capillary electrophoresis (CE) sepn. conditions for small, amine-contg. enantiomers. During method development, 39 pairs of enantiomers were studied and partial or complete sepn. was achieved in every case. Baseline resoln. was achieved by these initial screening conditions in over half of the cases. The screening strategy uses a bare fused silica capillary and a pH 2.5 amine-modified phosphate buffer contg. one of the selected cyclodextrins (CD): dimethyl-.beta.-CD, hydroxypropyl-.beta.-CD, hydroxypropyl-.alpha.-CD, hydroxypropyl-.gamma.-CD and sulfated-.beta.-CD. An addnl. set of compds. were screened by this approach to demonstrate the validity of the method. The paper outlines the exptl. work carried out to develop the screen and describes how one might implement it for a new compd.
IT **170566-83-3**
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process)
(systematic screening approach for chiral sepns. of amines by capillary electrophoresis using modified cyclodextrins)
RN 170566-83-3 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

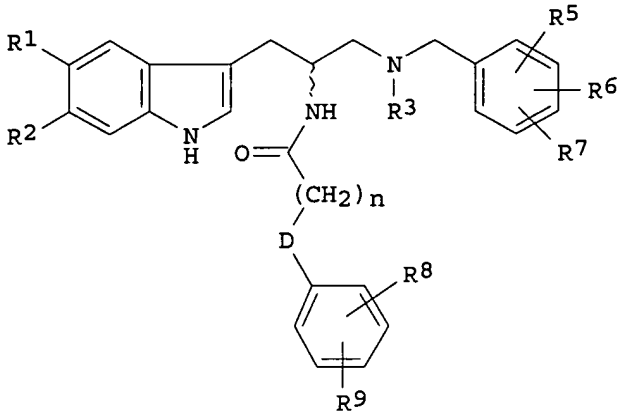


IT **170566-83-3 170566-84-4 170566-85-5**
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process)
(systematic screening approach for chiral sepns. of amines by capillary electrophoresis using modified cyclodextrins)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 28 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:182467 CA
TITLE: Preparation of 2-(acylamino)propanamines as tachykinin receptor antagonists
INVENTOR(S): Fritz, James Erwin; Hipskind, Philip Arthur; Kaldor, Stephen Warren; Lobb, Karen Lynn; Nixon, James Arthur
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9907677	A1	19990218	WO 1998-US16333	19980806
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886933	A1	19990301	AU 1998-86933	19980806
EP 1005454	A1	20000607	EP 1998-938403	19980806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9811821	A	20000815	BR 1998-11821	19980806
JP 2001512715	T2	20010828	JP 2000-506181	19980806
US 6358994	B1	20020319	US 2000-463855	20000127
NO 2000000519	A	20000331	NO 2000-519	20000201

PRIORITY APPLN. INFO.: US 1997-54997P P 19970806
WO 1998-US16333 W 19980806
OTHER SOURCE(S): MARPAT 130:182467
GI



I

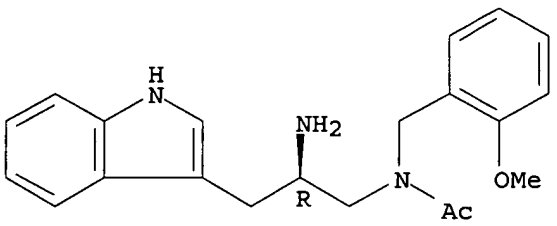
AB Nonpeptidyl 2-(acylamino)propanamines [I; R1, R2 = H, HO, halo, C1-6 alkyl, C1-6 alkoxy; R3 = H, C2-7 alkanoyl, (dimethyl)glycyl; R5-R7 = H, HO, halo, C1-6 alkyl, C1-6 alkoxy, CF3; R8, R9 = H, HO, C1-6 alkyl(thio), C1-6 alkoxy, C1-6 alkylamino, CF3O, CHO, cyano, pyrrolyl, imidazolyl, etc.; D = S(O)m, NH, CO, O; m = 0-2; n = 1-6], e.g., I [R1 = R2 = R6 = R7 = R8 = H, R3 = Ac, R5 = 2-MeO, R9 = 4-(1,2,3-thiadiazol-4-yl), D = O, n = 1], tachykinin receptor antagonists (no data) useful in the treatment of various conditions including Alzheimer's disease, were prepd., e.g., by amidation of (R)-2-amino-3-(1H-indol-3-yl)-1-[N-(2-methoxybenzyl)acetylamino]propane.cntdot.2HCl (4-step prepn. from L-tryptophan given). I, their **pharmaceutically** acceptable salts or solvates and **pharmaceutical** compns. contg. I were claimed.

IT **175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amidation; prepn. of 2-(acylamino)propanamines as tachykinin receptor antagonists)

RN 175460-99-8 CA

CN Acetamide, N-[(2R)-2-amino-3-(1H-indol-3-yl)propyl]-N-[(2-methoxyphenyl)methyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

IT **175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amidation; prepn. of 2-(acylamino)propanamines as

tachykinin receptor antagonists)

IT **175460-97-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deprotection; prepn. of 2-(acylamino)propanamines as tachykinin receptor antagonists)

IT **170566-88-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and etherification; prepn. of 2-(acylamino)propanamines as tachykinin receptor antagonists)

IT **170567-28-9P 220652-75-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-(acylamino)propanamines as tachykinin receptor antagonists)

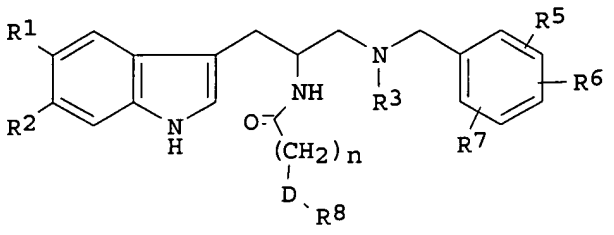
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 29 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:168238 CA
TITLE: 2-acylaminopropanamines as tachykinin receptor antagonists
INVENTOR(S): Fritz, James Erwin; Hipskind, Philip Arthur; Kaldor, Stephen Warren; Lobb, Karen Lynn; Nixon, James Arthur
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9907681	A1	19990218	WO 1998-US16313	19980806
W: AL, AM, AT, AU, AZ, BB, GB, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886926	A1	19990301	AU 1998-86926	19980806
EP 1003723	A1	20000531	EP 1998-938395	19980806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9811819	A	20000815	BR 1998-11819	19980806
JP 2001512717	T2	20010828	JP 2000-506185	19980806
US 6339094	B1	20020115	US 2000-463640	20000127
NO 2000000518	A	20000331	NO 2000-518	20000201

PRIORITY APPLN. INFO.: US 1997-55105P P 19970806
WO 1998-US16313 W 19980806

OTHER SOURCE(S): MARPAT 130:168238
GI



I

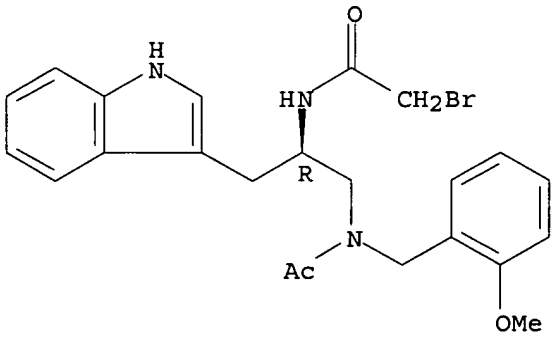
AB Title compds. [I; R1 and R2 are independently hydrogen, halo, alkyl, hydroxy, alkoxy; R3 is hydrogen, acetyl; alkanoyl, glycyl, dimethylglycyl; R5, R6, R7 are independently hydrogen, halo, alkyl alkoxy, trifluoromethyl hydroxy; n is 1-6; D is S(O)m, NH, O; m is 0, 1, 2; R8 is a monocyclic or bicyclic carbocyclic or heterocyclic group, optionally substituted with one or more moieties from the group consisting of oxo, alkyl, alkoxy, hydroxy, halo, and trifluoromethyl], or a **pharmaceutically** acceptable salt or solvate are prepd. in the presence of isocyanate resin polymer-bound coupling reagent 1-(3-dimethylaminoproyl)-3-propylcarbodiimide hydrochloride as tachykinin receptor antagonists and methods of treatment, **pharmaceutical** formulations are provided. Thus, (R)-I (R1 = H; R2 = H; R5 = 2-OMe; R6 = H; R7 = H; R8 = Br; D = electron pair; n = 1; R3 = Ac) were prepd.

IT **170566-88-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylaminopropanamines as tachykinin receptor antagonists)

RN 170566-88-8 CA

CN Acetamide, N-[(2R)-2-[(bromoacetyl)amino]-3-(1H-indol-3-yl)propyl]-N-[(2-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-88-8P 220441-63-4P 220441-64-5P**
220441-65-6P 220441-66-7P 220441-67-8P
220441-68-9P 220441-69-0P 220441-70-3P
220441-71-4P 220441-72-5P 220441-73-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylaminopropanamines as tachykinin receptor antagonists)

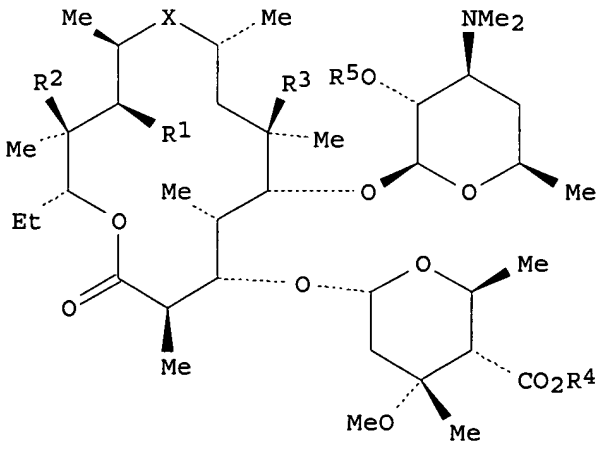
IT **175460-97-6P 175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(prepn. of acylaminopropanamines as tachykinin receptor antagonists)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 30 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:153920 CA
TITLE: Preparation of C-4" substituted macrolide erythromycin analogs as antibacterial and antiprotozoal agents
INVENTOR(S): Brighty, Katherine Elizabeth; Kaneko, Takushi; Linde, Robert Gerald, II; Masamune, Hiroko; McGuirk, Paul Robert; Su, Wei-guo; Wu, Yong-jin; Yang, Bingwei Vera
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 59 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 895999	A1	19990210	EP 1998-305956	19980727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6025350	A	20000215	US 1998-124408	19980729
CA 2244519	AA	19990206	CA 1998-2244519	19980805
JP 11116593	A2	19990427	JP 1998-232395	19980805
BR 9802851	A	20000829	BR 1998-2851	19980805
US 6300316	B1	20011009	US 1999-378886	19990823

PRIORITY APPLN. INFO.: US 1997-54866P P 19970806
US 1998-124408 A3 19980729
OTHER SOURCE(S): MARPAT 130:153920
GI



I

AB Macrolides I (X = CO, chain contg. substituted carbon and nitrogen; R1, R2 = independently OH; R1R2 = heterocycle; R3 = OH, OMe; R4 = aminoalkyl; R5 = H, acyl) were prepd. as antibacterial and antiprotozoal agents. The invention also relates to **pharmaceutical** compns. contg. the compds. of formula I and to methods of treating bacterial and protozoal

infections by administering the compds. of formula I. Thus, 4"-O-[2-(N,N-bis-2,4-dimethoxybenzyl)aminoethyl]aminocarbonylerythromycylamine was prepd. and tested for its antibacterial and antiprotozoal activities.

IT **220215-86-1P**

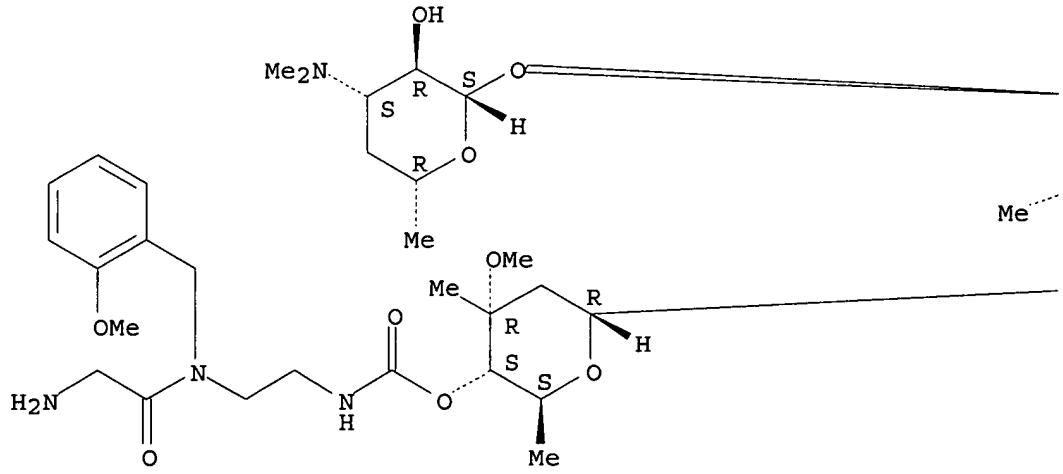
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of C-4'' substituted macrolide erythromycin analogs as antibacterial and antiprotozoal agents)

RN 220215-86-1 CA

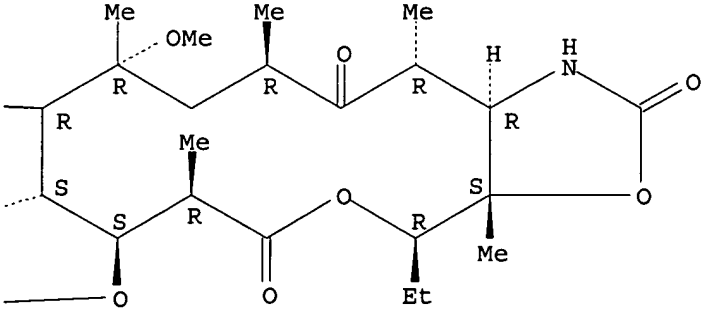
CN 2H-Oxacyclotetradecino[4,3-d]oxazole-2,6,14(1H,7H)-trione, 8-[[4-O-[[[2-[(aminoacetyl)[(2-methoxyphenyl)methyl]amino]ethyl]amino]carbonyl]-2,6-dideoxy-3-C-methyl-3-O-methyl-.alpha.-L-ribo-hexopyranosyl]oxy]-4-ethyldecahydro-11-methoxy-3a,7,9,11,13,15-hexamethyl-10-[[3,4,6-trideoxy-3-(dimethylamino)-.beta.-D-xylo-hexopyranosyl]oxy]-, (3aS,4R,7R,8S,9S,10R,11R,13R,15R,15aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT **220215-86-1P**

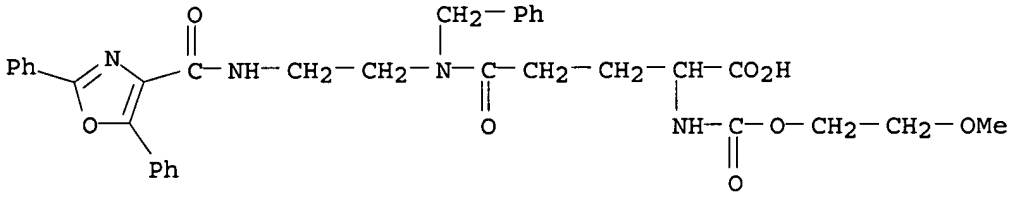
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of C-4'' substituted macrolide erythromycin analogs as antibacterial and antiprotozoal agents)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 31 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:119061 CA
TITLE: Disruption of insulin-like growth factor-1 signaling and down-regulation of Cdc2 by SC-.alpha..alpha..delta.9, a novel small molecule antisignaling agent identified in a targeted array library
AUTHOR(S): Vogt, Andreas; Rice, Robert L.; Settineri, Catherine E.; Yokokawa, Fumiaki; Yokokawa, Shiho; Wipf, Peter; Lazo, John S.
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 287(2), 806-813
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Lippencott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We previously reported the generation of a library of hydrophobic oxazole-based small mols. designed as inhibitors of phosphatases involved in cellular signaling and cell cycle control. One member of the targeted array library, 4-(benzyl-(2-[(2,5-diphenyl-oxazole-4-carbonyl)amino]ethyl)carbamoyl)-2-decanoylaminobutyric acid (SC-.alpha..alpha..delta.9), inhibited cell growth in the G0/G1 phase of the cell cycle. To investigate potential mechanisms for SC-.alpha..alpha..delta.9 antiproliferative activity, we have used mouse embryonic fibroblasts transformed with simian virus 40 large T antigen mouse embryonic fibroblasts as a model system for a malignant phenotype that depends on overexpression of cell cycle regulators and autocrine stimulation by insulin-like growth factor-1. Structure-activity relation studies with SC-.alpha..alpha..delta.9 and four library congeners demonstrated that antiproliferative activity was not a result of overall hydrophobicity. Rather, SC-.alpha..alpha..delta.9 decreased insulin-like growth factor-1 receptor tyrosine phosphorylation, receptor expression, mitogen-activated protein kinase activation and levels of the cyclin-dependent kinase Cdc2. Less toxic congeners only partially affected receptor expression, receptor tyrosine phosphorylation and Cdc2 levels. Thus SC-.alpha..alpha..delta.9, which is structurally distinct from other known small mols. that decrease intracellular Cdc2 levels, has profound effects on intracellular signaling. Furthermore, SC-.alpha..alpha..delta.9, but not vanadate or okadaic acid, selectively inhibited the growth of simian virus 40 large T antigen mouse embryonic fibroblasts compared to the parental cells. These results suggest that overexpression of Cdc2 and increased dependence on insulin-like growth factor-1 autocrine stimulation are responsible for the increased sensitivity of simian virus 40 large T antigen mouse embryonic fibroblasts to SC-.alpha..alpha..delta.9. The SC-.alpha..alpha..delta.9 **pharmacophore** could be a useful platform for the development of novel antisignaling agents.
IT **219857-86-0**, SC-.alpha..alpha..delta.4II
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(disruption of insulin-like growth factor-1 signaling and down-regulation of Cdc2 by SC-.alpha..alpha..delta.9, a novel small mol. antisignaling agent identified in a targeted array library)

RN 219857-86-0 CA

CN Glutamine, N-[2-[[(2,5-diphenyl-4-oxazolyl)carbonyl]amino]ethyl]-N2-[(2-methoxyethoxy)carbonyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT **219857-86-0**, SC-.alpha..alpha..delta.4II **219905-91-6**, SC-.alpha..alpha..delta.9 **219905-92-7**, SC-.alpha..alpha..delta.6III

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(disruption of insulin-like growth factor-1 signaling and down-regulation of Cdc2 by SC-.alpha..alpha..delta.9, a novel small mol. antisignaling agent identified in a targeted array library)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 32 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 130:95560 CA

TITLE: Preparation of barbituric acid derivatives with antimetastatic and antitumor activity

INVENTOR(S): Oliva, Ambrogio; De Cillis, Gianpiero; Grams, Frank; Livi, Valeria; Zimmermann, Gerd; Menta, Ernesto; Krell, Hans-Willi

PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany

SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

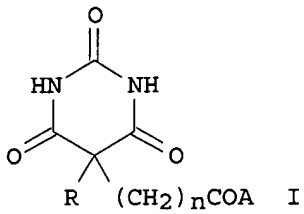
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858925	A1	19981230	WO 1998-EP3677	19980618
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9885391	A1	19990104	AU 1998-85391	19980618
AU 746853	B2	20020502		
EP 989982	A1	20000405	EP 1998-936361	19980618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9810450	A	20000905	BR 1998-10450	19980618
JP 2002504916	T2	20020212	JP 1999-503748	19980618

ZA 9805352 A 19991220 ZA 1998-5352 19980619
US 6335332 B1 20020101 US 2000-445461 20000403
PRIORITY APPLN. INFO.: EP 1997-110200 A 19970621
WO 1998-EP3677 W 19980618
OTHER SOURCE(S): MARPAT 130:95560
GI



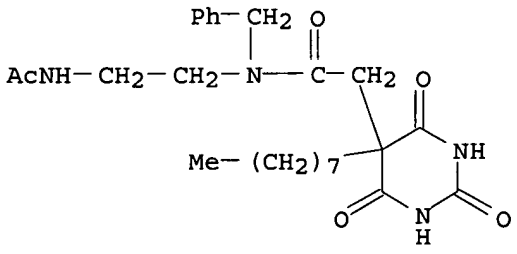
I

AB The title compds. [I; R = WV; A = R1, NR2(CH2)mNR9TR10, etc.; R1 = OH, C1-4 alkoxy, NH2, mono- or di(C1-4 alkyl)amino, (un)substituted phenoxy, benzyloxy, etc.; R9, R10 = H, (un)substituted C1-4 alkyl, Ph, etc.; R9R10NCO may form a 5- or 6-membered lactam ring; T = CO, SO2; V = (un)substituted (un)satd. mono- or bicyclic group optionally contg. 1-3 N, O, S; W = bond, C1-8 alkyl, C2-8 alkenyl; n = 1-3] as enantiomers, racemates, diastereoisomers, tautomers or their mixts., and their **pharmaceutically** acceptable salts, inhibitors of the metzincins useful for the title purpose, were prepd. For example, cyclocondensation of urea with di-Et 2-octylmalonate (prepn. by alkylation of di-Et malonate with 1-bromooctane given) gave 5-octylbarbituric acid which was alkylated with BrCH2CO2Et in DMF in the presence of Na2CO3 to give 5-octyl-5-(ethoxycarbonylmethyl)barbituric acid. The latter in vitro inhibited human neutrophil collagenase (MMP-8) with IC50 107 nM and gelatinase 92 kD (MMP-9) with IC50 19.6 nM which gave selectivity (MMP-9/MMP-8) ratio of 0.18-0.2, vs. 0.93 for batimastat as a ref. Approx. 6 I were prepd. and approx. 21 I were claimed.

IT **219310-92-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of barbituric acid derivs. with antimetastatic and antitumor activity)

RN 219310-92-6 CA

CN 5-Pyrimidineacetamide, N-[2-(acetylamino)ethyl]hexahydro-5-octyl-2,4,6-trioxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



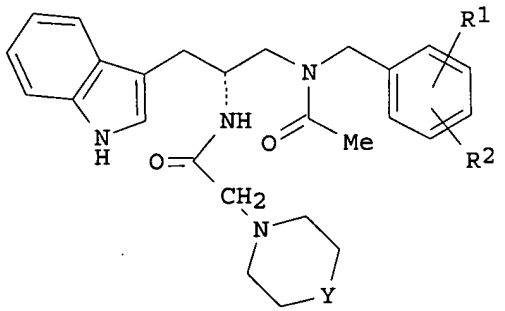
IT **219310-92-6P 219310-93-7P 219310-96-0P**

219310-97-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of barbituric acid derivs. with antimetastatic and antitumor activity)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 33 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:33026 CA
TITLE: Tachykinin receptor antagonists for treatment of pulmonary hypertension
INVENTOR(S): Gehlert, Donald Richard; Steinberg, Mitchell Irvin
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5846973	A	19981208	US 1997-862709	19970523

PRIORITY APPLN. INFO.: US 1997-862709 19970523
GI



I

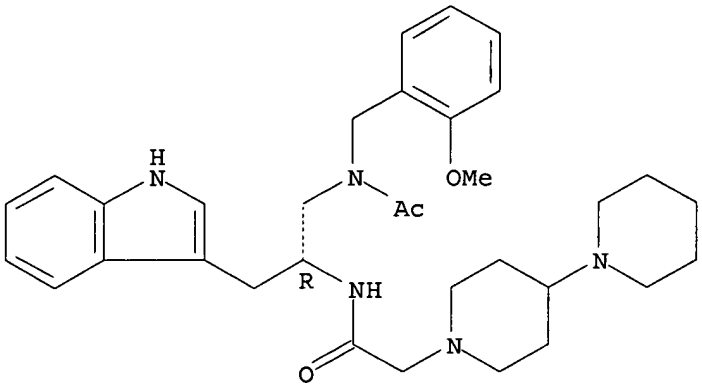
AB This invention provides methods of inhibiting pulmonary hypertensive disease which comprise administering to a mammal in need thereof a compd. having activity as a tachykinin receptor antagonist. A most preferred class of tachykinin receptor antagonists are compds. of the structure (I; R1, R2 = H, Me, OMe, Cl, CF3; Y = CHR3, NR3; R3 = cyclohexyl, piperidyl, Ph). I (R1 = 2-OMe, R2 = H, Y = CHR3; R3 = piperidyl) was prepd. and tested for binding to NK1 and NK2 receptors. Various formulations of tachykinin receptor antagonists, such as capsules, tablets, dry powder inhaler, suppositories, etc., were proposed.

IT **167678-33-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin receptor antagonists for treatment of pulmonary hypertension)
RN 167678-33-3 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-

methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]-, dihydrochloride, trihydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



●2 HCl

PAGE 2-A

●3 H_2O

IT **167678-33-3P 170566-84-4P 170567-08-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin receptor antagonists for treatment of pulmonary hypertension)

IT **175460-97-6P 175460-98-7P 175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tachykinin receptor antagonists for treatment of pulmonary hypertension)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 34 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:286003 CA
TITLE: Methods using tachykinin receptor antagonists for treating bone loss, conditions associated with a lack of parathyroid hormone, and hyperparathyroidism
INVENTOR(S): Galvin, Rachelle Jeanette; Gitter, Bruce Donald
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843639	A1	19981008	WO 1998-US6674	19980403
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9868833	A1	19981022	AU 1998-68833	19980403
US 6239144	B1	20010529	US 1999-319388	19990527
PRIORITY APPLN. INFO.:			US 1997-43909P P	19970403
			WO 1998-US6674 W	19980403

AB The present invention provides methods of treating or preventing conditions assocd. with a lack of parathyroid hormone comprising administering to a mammal in need thereof an effective amt. of a compd. having activity as a tachykinin receptor antagonist. In a most preferred embodiment the present invention provides methods of increasing bone growth in a mammal which comprises administering to a mammal in need thereof an effective amt. of a compd. having activity as a tachykinin receptor antagonist. Another embodiment of this invention provides methods of treating hyperparathyroidism in a mammal comprising administering to a mammal in need thereof an effective amt. of a compd. having activity as a tachykinin receptor antagonist.

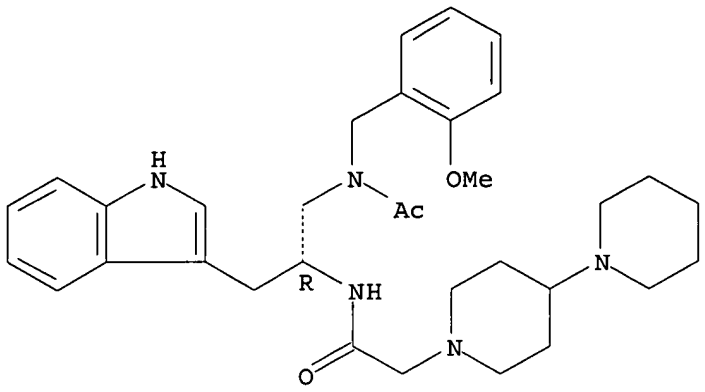
IT **167678-33-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tachykinin receptor antagonists for treating bone loss, conditions assocd. with a lack of parathyroid hormone, and hyperparathyroidism)

RN 167678-33-3 CA

CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]-, dihydrochloride, trihydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



●2 HCl

PAGE 2-A

●3 H_2O

IT **167678-33-3 170566-84-4 170567-08-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tachykinin receptor antagonists for treating bone loss, conditions assocd. with a lack of parathyroid hormone, and hyperparathyroidism)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 35 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:285918 CA
TITLE: Selective neurokinin-1 receptor antagonists are anti-hyperalgesic in a model of neuropathic pain in the guinea pig
AUTHOR(S): Campbell, E. A.; Gentry, C. T.; Patel, S.; Panesar, M. S.; Walpole, C. S. J.; Urban, L.
CORPORATE SOURCE: Novartis Institute for Medical Sciences, London, WC1E 6BN, UK
SOURCE: Neuroscience (Oxford) (1998), 87(3), 527-532
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neuropathic pain is poorly managed by conventional analgesic therapy, such as non-steroidal anti-inflammatory drugs and opiates. The development of animal models of peripheral neural damage has aided in our understanding of the pathol. and **pharmacol**. of neuropathic pain. This report is the first clear demonstration using selective neurokinin-1 receptor antagonists of a potentially novel therapeutic approach to the treatment of neuropathic pain resulting from peripheral nerve damage in a guinea-pig model. The neurokinin-1 receptor antagonists, SDZ NKT 343 and LY 303870

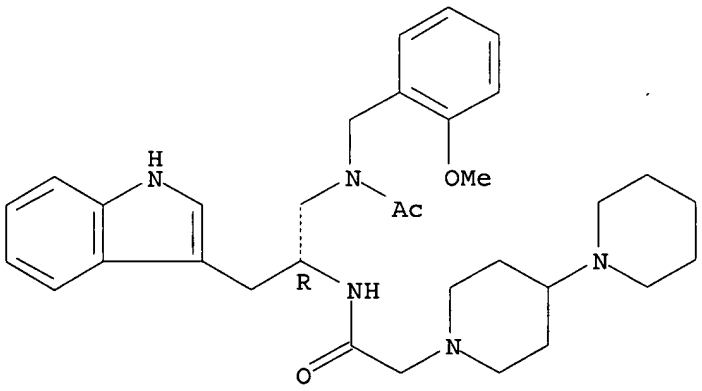
significantly reduced mech. hyperalgesia following oral and intrathecal administration. (R,R)-SDZ NK T343, the enantiomer of SDZ NKT 343 did not show anti-hyperalgesic activity. RPR 100893 showed significant antihyperalgesic activity only following intrathecal administration suggesting poor absorption or low level penetration of the blood-brain barrier. These results imply that neurokinin-1 receptor antagonists offer a new class of anti-hyperalgesic drugs with a largely central site of action in neuropathic pain.

IT **170566-84-4**, LY 303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective NK1 receptor antagonists are anti-hyperalgesic in model of neuropathic pain in the guinea pig)

RN 170566-84-4 CA

CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4**, LY 303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective NK1 receptor antagonists are anti-hyperalgesic in model of neuropathic pain in the guinea pig)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 36 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 129:41128 CA

TITLE: Preparation of heterocyclic [and particularly imidazole-containing] low molecular weight peptidyl compounds as inhibitors of farnesyl-protein transferase

INVENTOR(S): Anthony, Neville J.; Bergman, Jeffrey M.; Dinsmore, Chrisopher J.; Gomez, Robert P.; MacTough, Suzanne C.; Solinsky, Kelly M.; Williams, Theresa M.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

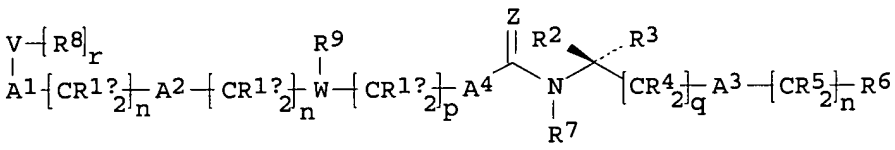
SOURCE: U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 468,160, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

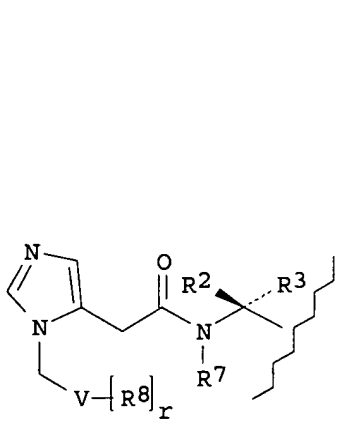
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5756528	A	19980526	US 1996-652055	19960523
CA 2223561	AA	19961212	CA 1996-2223561	19960603
US 5972984	A	19991026	US 1997-960248	19971029

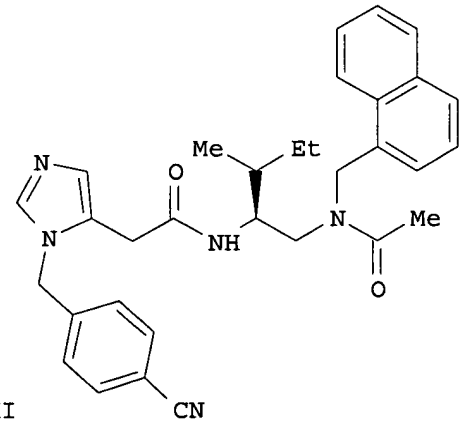
PRIORITY APPLN. INFO.: US 1995-468160 19950606
US 1996-652055 19960523
OTHER SOURCE(S): MARPAT 129:41128
GI



I



II



III

AB The invention comprises low mol. wt. peptidyl compds. that inhibit the enzyme farnesyl-protein transferase (FPTase). The compds. differ from prior mono- or dipeptidyl analogs previously described as FPTase inhibitors by lacking a thiol moiety. This offers unique advantages (no data) in terms of improved **pharmacokinetic** behavior in animals, prevention of thiol-dependent chem. reactions, such as rapid autoxidn. and disulfide formation with endogenous thiols, and reduced systemic toxicity. Further contained in the invention are chemotherapeutic compns. contg. the compds., and methods for their prodn. A method of inhibition of FPTase by administration of I [R1a = H, aryl, heterocycle, etc.; R1b = H, (un)substituted aryl, heterocycle, etc.; R2, R3 = a side chain of a naturally occurring amino acid, (un)substituted C1-20 alkyl, etc.; R4, R5 = H, (un)substituted C1-6 alkyl, aryl, etc.; R6 = H, aryl, C3-10 cycloalkyl, etc.; R7 = H, (un)substituted aryl, heterocyclyl, etc.; R8 = H, (un)substituted aryl, heterocyclyl, etc.; R9 = H, C2-20 alkenyl, C2-20 alkynyl, etc.; A1-A3 = bond, CH:CH, C.tplbond.C, etc.; A4 = bond, NR7, S, O; V = H, heterocycle, aryl, etc.; W = heterocycle; Z = O, (R1a)2; n, p, q = 0-4; r = 0-5] is claimed. The subset of imidazole compds. II and their **pharmaceutically** acceptable salts, which inhibit Ras

farnesyl-transferase, are also claimed per se. For instance, EDC-mediated coupling of N-allyloxycarbonyl-N-(naphth-1-ylmethyl)-2(S)-amino-3(S)-methylpentanamine.HCl with [1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetic acid, followed by Pd-catalyzed deallyloxycarbonylation, and acetylation with AcCl, gave the claimed title compd. III, which was isolated as a trifluoroacetate salt. The compds. showed IC50 values of < 50 .mu.M against human FPTase.

IT **186199-44-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocycle-contg. low mol. peptidyl compds. as inhibitors of farnesyl-protein transferase)

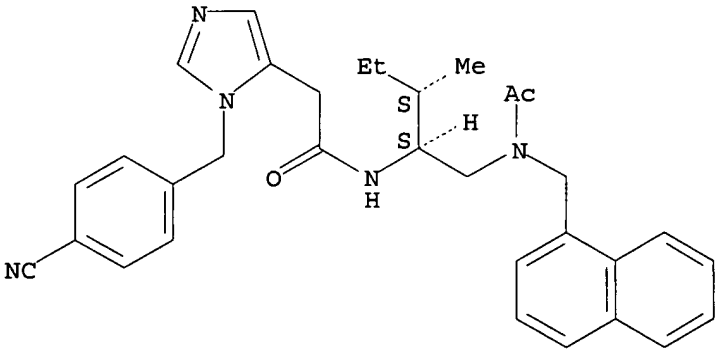
RN 186199-44-0 CA

CN 1H-Imidazole-5-acetamide, N-[(1S,2S)-1-[[acetyl(1-naphthalenylmethyl)amino]methyl]-2-methylbutyl]-1-[(4-cyanophenyl)methyl]-, trifluoroacetate (2:5) (9CI) (CA INDEX NAME)

CM 1

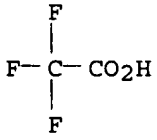
CRN 186199-43-9
CMF C32 H35 N5 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **186199-44-0P 186199-46-2P 186201-10-5P 186201-11-6P 186201-13-8P 186201-14-9P 186201-15-0P 186201-18-3P 186201-19-4P 186201-61-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heterocycle-contg. low mol. peptidyl compds. as inhibitors of farnesyl-protein transferase)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 37 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:23447 CA
TITLE: A method for treating tension-type headache
INVENTOR(S): Olesen, Jes; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf
PATENT ASSIGNEE(S): Olesen, Jes, Den.; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819674	A2	19980514	WO 1997-DK502	19971104
WO 9819674	A3	19980716		
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, ES, FI, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748632	A1	19980529	AU 1997-48632	19971104
AU 734490	B2	20010614		
EP 1011656	A2	20000628	EP 1997-911150	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1132082	A1	20010912	EP 2000-204625	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6284794	B1	20010904	US 1999-304115	19990504
US 2002072543	A1	20020613	US 2001-941855	20010830

PRIORITY APPLN. INFO.:

DK 1996-1243	A	19961105
US 1996-30294P	P	19961105
EP 1997-911150	A3	19971104
WO 1997-DK502	W	19971104
US 1998-85413P	P	19980514
US 1999-304115	A3	19990504

AB Tension-type headache is treated by interacting with neuronal transmission in relation to pain in connection with headache in a way which prevents or decreases sensitization of second order nociceptive neurons. In particular, treatment is performed by administration of an effective amt. of a substance which prevents or decreases central sensitization. Important examples of such substances are substances which interact with glutamate neurotransmission, such as glutamate receptor antagonists. Other examples are e.g. substances which interact with nitric oxide, such as nitric oxide synthase (NOS) inhibitors. According to a broader aspect of the invention, tension-type headache is treated by administration of substances which are effective in preventing or decreasing pain in connection with tension-type headache. An addnl. aspect of the invention

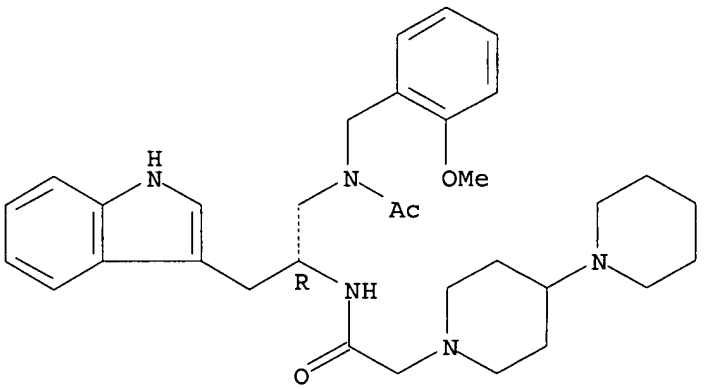
relates to treatment of tension-type headache by administration of substances which substantially inhibit the activity of NOS. Evidence for central sensitization in chronic myofascial pain, as well as mechanisms of spontaneous tension-type headaches, are also described. Gabapentin and dextromethorphen had a prophylactic effect on chronic tension-type headaches.

IT **170566-84-4**, LY 303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tension-type headache treatment)

RN 170566-84-4 CA

CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4**, LY 303870 **170566-84-4D**, LY 303870, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tension-type headache treatment)

L15 ANSWER 38 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 128:72247 CA

TITLE: A Targeted Library of Small-Molecule, Tyrosine, and Dual-Specificity Phosphatase Inhibitors Derived from a Rational Core Design and Random Side Chain Variation

AUTHOR(S): Rice, Robert L.; Rusnak, James M.; Yokokawa, Fumiaki; Yokokawa, Shiho; Messner, Donald J.; Boynton, Alton L.; Wipf, Peter; Lazo, John S.

CORPORATE SOURCE: Departments of Pharmacology and Chemistry, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Biochemistry (1997), 36(50), 15965-15974
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tyrosine phosphatases (PTPases) dephosphorylate phosphotyrosines while dual-specificity phosphatases (DSPases) dephosphorylate contiguous and semicontiguous phosphothreonine and phosphotyrosine on cyclin dependent kinases and mitogen-activated protein kinases. Consequently, PTPases and DSPases have a central role controlling signal transduction and cell cycle

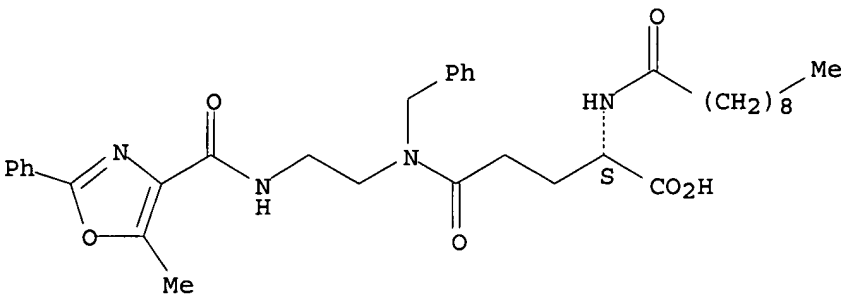
progression. Currently, there are few readily available potent inhibitors of PTPases or DSPases other than vanadate. Using a **pharmacophore** modeled on natural product inhibitors of phosphothreonine phosphatases, the authors generated a refined library of novel, phosphate-free, small-mol. compds. synthesized by a parallel, solid-phase combinatorial-based approach. Among the initial 18 members of this targeted diversity library, the authors identified several inhibitors of DSPases: Cdc25A, -B, and -C and the PTPase PTP1B. These compds. at 100 .mu.M did not significantly inhibit the protein serine/threonine phosphatases PP1 and PP2A. Kinetic studies with two members of this library indicated competitive inhibition for Cdc25 DSPases and noncompetitive inhibition for PTP1B. Compd. AC-.alpha..alpha.69 had a Ki of approx. 10 .mu.M for recombinant human Cdc25A, -B, and -C, and a Ki of 0.85 .mu.M for the PTP1B. The marked differences in Cdc25 inhibition as compared to PTP1B inhibition seen with relatively modest chem. modifications in the modular side chains demonstrate the structurally demanding nature of the DSPase catalytic site distinct from the PTPase catalytic site. These results represent the first fundamental advance toward a readily modifiable **pharmacophore** for synthetic PTPase and DSPase inhibitors and illustrate the significant potential of a combinatorial-based strategy that supplements the rational design of a core structure by a randomized variation of peripheral substituents.

IT **188403-16-9**, AC-.alpha.1.delta.9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(library of small-mol. phosphatase inhibitors with specificity for cyclin-dependent kinase phosphatases and mitogen-activated protein kinase phosphatases)

RN 188403-16-9 CA

CN L-Glutamine, N-[2-[[(5-methyl-2-phenyl-4-oxazolyl)carbonyl]amino]ethyl]-N2-(1-oxodecyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **188403-16-9**, AC-.alpha.1.delta.9 **188403-19-2**, AC-.alpha..alpha..delta.9 **188403-22-7**, AC-.alpha.1.delta..beta. **188403-27-2**, AC-.alpha..alpha..delta..beta. **188403-36-3**, AC-.alpha.1.delta..gamma. **188403-42-1**, AC-.alpha..alpha..delta..gamma.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(library of small-mol. phosphatase inhibitors with specificity for cyclin-dependent kinase phosphatases and mitogen-activated protein kinase phosphatases)

L15 ANSWER 39 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:53244 CA

TITLE: Methods of treating hypertension
INVENTOR(S): Gehlert, Donald R.; Steinberg, Mitchell I.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Gehlert, Donald R.; Steinberg, Mitchell I.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744035	A1	19971127	WO 1997-US9225	19970523
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9731492	A1	19971209	AU 1997-31492	19970523
EP 912178	A1	19990506	EP 1997-926817	19970523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2000511193	T2	20000829	JP 1997-542963	19970523

PRIORITY APPLN. INFO.: US 1996-18266P P 19960524
WO 1997-US9225 W 19970523

OTHER SOURCE(S): MARPAT 128:53244

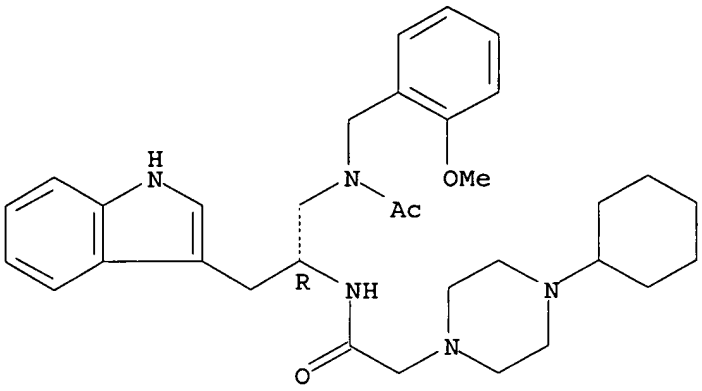
AB This invention provides methods of inhibiting pulmonary hypertensive disease which comprise administering to a mammal in need thereof a compd. having activity as a tachykinin receptor antagonist. One of the example compds. prepd. is (R)-2-[N-[2-[(4-cyclohexyl)piperazin-1-yl]acetyl]amino]-3-(1H-indol-3-yl)-1-[N-(2-methoxybenzyl)acetylamino]propane. Tests for antihypertensive activity are also given.

IT **170567-08-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin receptor antagonists as antihypertensives)

RN 170567-08-5 CA

CN 1-Piperazineacetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]-4-cyclohexyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170567-08-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin receptor antagonists as antihypertensives)

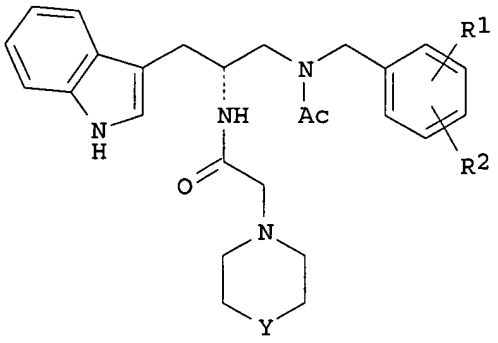
IT **167678-33-3P 175460-97-6P 175460-98-7P 175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tachykinin receptor antagonists as antihypertensives)

IT **170566-84-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin receptor antagonists as antihypertensives)

L15 ANSWER 40 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:293251 CA
TITLE: Methods of treating or preventing interstitial cystitis using piperazinyl- and piperidinyl-containing indole derivatives
INVENTOR(S): Iyengar, Smriti; Muhlhauser, Mark A.; Thor, Karl B.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Iyengar, Smriti; Muhlhauser, Mark A.; Thor, Karl B.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733583	A1	19970918	WO 1997-US3555	19970307
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2247822	AA	19970918	CA 1997-2247822	19970307
AU 9720714	A1	19971001	AU 1997-20714	19970307

EP 932406 A1 19990804 EP 1997-908927 19970307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
JP 2000506527 T2 20000530 JP 1997-532693 19970307
US 6017930 A 20000125 US 1998-125952 19980825
PRIORITY APPLN. INFO.: US 1996-13130P P 19960311
WO 1997-US3555 W 19970307
OTHER SOURCE(S): MARPAT 127:293251
GI



I

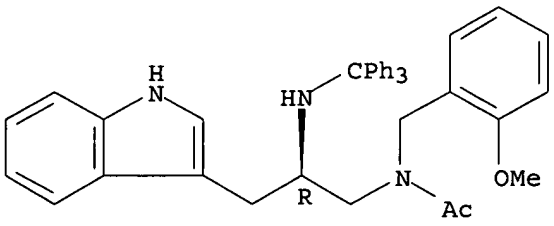
AB The invention provides methods for the treatment or prevention of interstitial cystitis or urethral syndrome using compds. I [R1, R2 = H, Me, OMe, Cl, CF3, with the proviso that only 1 may be H; Y = NR, CHR, NRa, or CHNRbRc; R = cyclohexyl, piperidino, or Ph; Ra, Rb, Rc = H, C1-6 alkyl] or their **pharmaceutically** acceptable salts or solvates. Detailed prepns. of 2 compds. and some of their salts are given. For instance, Ph3C-D-Trp-OH underwent a sequence of amidation with 2-MeOC6H4CH2NH2 (95%), redn. of the amide to an amine using RED-AL.RTM. and then N-acetylation using Ac2O (87%), detritylation (90%), conversion to the di-HCl salt (>98%), and finally amidation with 2-(4-cyclohexylpiperazin-1-yl)acetic acid K salt, to give title compd. I [R1 = 2-OMe, R2 = H, Y = NR, R = cyclohexyl]. Relevant methods for bioassay and clin. evaluation of the compds. are also described (no data).

IT **175460-97-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of piperazinyl- and piperidinyl-contg. indole derivs. for treatment of interstitial cystitis)

RN 175460-97-6 CA

CN Acetamide, N-[(2R)-3-(1H-indol-3-yl)-2-[(triphenylmethyl)amino]propyl]-N-[(2-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **175460-97-6P 175460-98-7P 175460-99-8P**

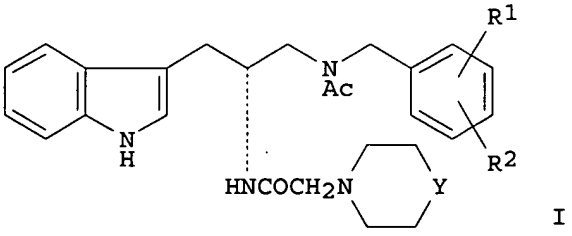
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of piperazinyl- and piperidinyl-contg. indole derivs. for treatment of interstitial cystitis)

IT **170508-05-1P 170566-84-4P 170567-08-5P 188949-24-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazinyl- and piperidinyl-contg. indole derivs. for treatment of interstitial cystitis)

L15 ANSWER 41 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:176440 CA
TITLE: Indolylpropanediamine derivatives as tachykinin antagonists
INVENTOR(S): Iyengar, Smriti; Phebus, Lee A.; Shannon, Harlan E.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Iyengar, Smriti; Phebus, Lee A.; Shannon, Harlan E.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9725988	A1	19970724	WO 1997-US788	19970117
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9722438	A1	19970811	AU 1997-22438	19970117

PRIORITY APPLN. INFO.: US 1996-10133P P 19960117
WO 1997-US788 W 19970117
OTHER SOURCE(S): MARPAT 127:176440
GI



I

AB Title compds. I [R1, R2 = H, Me, OMe, Cl, CF3; Y = NR3, CHR3; R3 = cyclohexyl, piperidino, Ph, H, alkyl, amino] were prepd. for use as tachykinin antagonists, optionally in combination with non-tachykinin

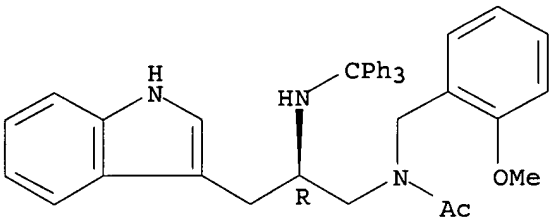
antagonist analgesics. **Pharmaceutical** formulations are also reported. Thus, I [Y = NR3, R1 = 2-OMe, R2 = H, R3 = cyclohexyl] was prepd. from D-tryptophan in 7 steps.

IT **175460-97-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of indolylpropanediamine derivs. as tachykinin antagonists)

RN 175460-97-6 CA

CN Acetamide, N-[(2R)-3-(1H-indol-3-yl)-2-[(triphenylmethyl)amino]propyl]-N-[(2-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **175460-97-6P 175460-98-7P 175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of indolylpropanediamine derivs. as tachykinin antagonists)

IT **170508-05-1P 170566-84-4P 170567-08-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indolylpropanediamine derivs. as tachykinin antagonists)

L15 ANSWER 42 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 127:34521 CA

TITLE: Preparation of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors

INVENTOR(S): Carr, Thomas Joseph; Desjarlais, Renee Louise; Gallagher, Timothy Francis; Halbert, Stacie Marie; Oh, Hye-Ja; Thompson, Scott Kevin; Veber, Daniel Frank; Yamashita, Dennis Shinji; et al.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 253 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716433	A1	19970509	WO 1996-US18000	19961030
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9609078	A	19980429	ZA 1996-9078	19961029
AU 9711180	A1	19970522	AU 1997-11180	19961030

CN 1207095	A	19990203	CN 1996-199284	19961030	
BR 9612344	A	19990713	BR 1996-12344	19961030	
EP 934291	A1	19990811	EP 1996-941981	19961030	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO					
NO 9801938	A	19980629	NO 1998-1938	19980429	
US 5998470	A	19991207	US 1999-290958	19990413	
US 6057362	A	20000502	US 1999-330287	19990611	
US 6232342	B1	20010515	US 1999-330451	19990611	
US 6284777	B1	20010904	US 2000-552616	20000419	
US 6331542	B1	20011218	US 2000-551968	20000419	
NO 2000006716	A	19980629	NO 2000-6716	20001229	
NO 2000006717	A	19980629	NO 2000-6717	20001229	
NO 2000006718	A	19980629	NO 2000-6718	20001229	
CN 1341590	A	20020327	CN 2001-104787	20010220	
CN 1341592	A	20020327	CN 2001-104788	20010220	
CN 1341593	A	20020327	CN 2001-104789	20010220	
US 2002077455	A1	20020620	US 2001-839410	20010420	
US 2002173469	A1	20021121	US 2002-160314	20020530	
PRIORITY APPLN. INFO.:			US 1995-8108P	P	19951030
			US 1995-7473P	P	19951122
			US 1995-8992P	P	19951221
			US 1996-13747P	P	19960320
			US 1996-13748P	P	19960320
			US 1996-13764P	P	19960320
			US 1996-17455P	P	19960517
			US 1996-17892P	P	19960517
			US 1996-22047P	P	19960722
			US 1996-23494P	P	19960807
			WO 1996-US18000	W	19961030
			US 1997-793915	A3	19970214
			US 1998-793915	B3	19980430
			US 1999-330284	B1	19990611
			US 1999-330305	B1	19990611
			US 2000-633700	B1	20000807

OTHER SOURCE(S): MARPAT 127:34521

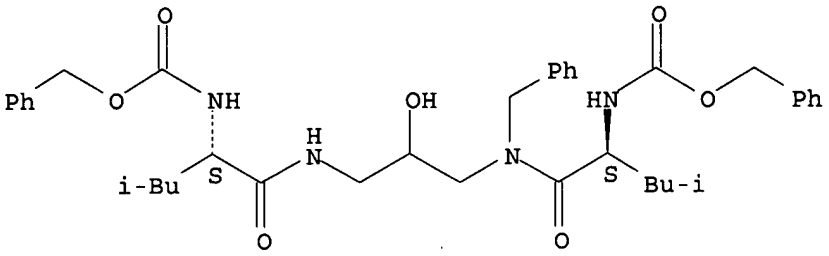
AB Title compds. of formula D-CO-Q [D = CbzNHCH(Bu-i), Cbz-Leu-NHCH(Bu-i), 4-PhOC6H4SO2NHCH2, Cbz-Leu-NHNH, etc.; Q = NHCH(Bu-i)(2-carboxythiazol-4-yl), NHCH(Bu-i)(4-carboethoxythiazol-2-yl), NHNHCOCH(Bu-i)NHCbz, CH2NHSO2C6H4-4-OPh, etc.; Cbz = PhCH2O2C] and **pharmaceutical** compns. of such compds., which inhibit proteases, including cathepsin K (no data) were prepd. Such compds. are particularly useful for treating diseases of excessive bone loss or cartilage or matrix degrdn., e.g. osteoporosis, periodontitis, and arthritis. For example, Cbz-Leu-Leu-CH2Br was treated with H2NCSCO2Et in refluxing ethanol for 4 h to give Cbz-Leu-NHCH(Bu-i)(2-carboethoxythiazol-4-yl), which was sapond. by treatment with sodium hydroxide in THF to yield title compd. Cbz-Leu-NHCH(Bu-i)(2-carboxythiazol-4-yl).

IT **190660-88-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors)

RN 190660-88-9 CA

CN 2,5,9,12-Tetraazatridecanedioic acid, 7-hydroxy-3,11-bis(2-methylpropyl)-4,10-dioxo-5-(phenylmethyl)-, bis(phenylmethyl) ester, (3S,11S)-[partial]- (9CI) (CA INDEX NAME)

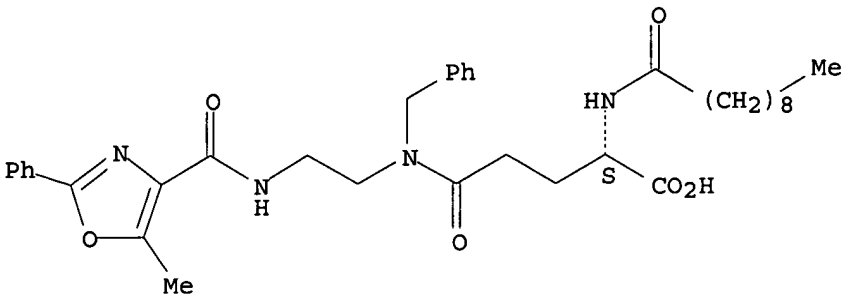
Absolute stereochemistry.



IT **190660-88-9P 190900-99-3DP**, resin-bound
190901-05-4DP, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors)

L15 ANSWER 43 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:220304 CA
TITLE: Combinatorial synthesis and biological evaluation of library of small-molecule Ser/Thr-protein phosphatase inhibitors
AUTHOR(S): Wipf, Peter; Cunningham, April; Rice, Robert L.; Lazo, John S.
CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SOURCE: Bioorganic & Medicinal Chemistry (1997), 5(1), 165-177
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In eukaryotes, phosphorylation of serine, threonine, and tyrosine residues on proteins is a fundamental post-translational regulatory process for such functions as signal transduction, gene transcription, RNA splicing, cellular adhesion, apoptosis, and cell cycle control. Based on functional groups present in natural product serine/threonine protein phosphatase (PSTPase) inhibitors, we have designed **pharmacophore** model and demonstrated the feasibility of a combinatorial chem. approach for the prepn. of functional analogs of the model. Preliminary biol. testing of 18 structural variants of the model has identified two compds. with growth inhibitory activity against cultured human breast cancer cells. In vitro inhibition of the PSTPase PP2A was demonstrated with one of the compds. Using flow cytometry, it was obsd. that one compd. caused prominent inhibition in the G1 phase of the cell cycle. Thus, the combinatorial modifications of the minimal **pharmacophore** can generate biol. interesting antiproliferative agents.
IT **188403-16-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(combinatorial synthesis and biol. evaluation of library of small-mol. Ser/Thr-protein phosphatase inhibitors)
RN 188403-16-9 CA
CN L-Glutamine, N-[2-[[(5-methyl-2-phenyl-4-oxazolyl)carbonyl]amino]ethyl]-N2-(1-oxodecyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **188403-16-9P 188403-19-2P 188403-22-7P**
188403-27-2P 188403-36-3P 188403-42-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(combinatorial synthesis and biol. evaluation of library of small-mol. Ser/Thr-protein phosphatase inhibitors)

L15 ANSWER 44 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:195101 CA
TITLE: Peripheral effects of three novel non-peptide tachykinin NK1 receptor antagonists in the anesthetized rat
AUTHOR(S): Cellier, Eric; Fayolle, Christine; Hipskind, Philip A.; Iyengar, Smriti; Couture, Rejean
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine, Universite de Montreal, C.P. 6128, Succursale Centre-Ville, Montreal, Quebec, Can.
SOURCE: European Journal of Pharmacology (1996), 318(2/3), 377-385
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three novel non-peptide tachykinin NK1 receptor antagonists were assessed on the transient fall in mean arterial blood pressure and the salivation induced by i.v. substance P (0.65 nmol/kg) in the urethane-anesthetized rat. LY303241 ((R)-1-[N-(2-methoxybenzyl)acetylamino]-3-(1H-indol-3-yl)-2-[N-(2-(4-phenylpiperazin-1-yl)acetyl)amino]propane), LY303870 ((R)-1-[N-(2-methoxybenzyl)acetylamino]-3-(1H-indol-3-yl)-2-[N-(2-(4-(piperidin-1-yl)piperidin-1-yl)acetyl)amino]propane) and LY306740 ((R)-1-[N-(2-methoxybenzyl)acetylamino]-3-(1H-indol-3-yl)-2-[N-(2-(4-cyclohexylpiperazin-1-yl)acetyl)amino]propane) (65 nmol-9 .mu.mol/kg i.v.; 5 min earlier) inhibited both the vasodepressor and salivary responses to substance P in a dose-dependent manner. LY303241 and LY306740 were more potent in inhibiting the vascular response to substance P while LY303870 was more potent in inhibiting the salivary response. LY303870 and LY306740 were devoid of direct effects while LY303241 decreased blood pressure and heart rate for 1 and 10 min, resp. The antagonists act in a stereoselective and specific manner since the opposite (S) enantiomers of LY303870 (LY306155) and LY306740 (LY307679) failed to block the effects of substance P. In addn., LY303241, LY303870 and LY306740 neither affected the hypotension and the salivation induced by carbachol nor the increases in mean arterial pressure and heart rate induced by the tachykinin NK receptor agonist [-Ala]neurokinin A-(4-10). Only LY303241 attenuated the decreases in mean arterial pressure and heart rate evoked by the

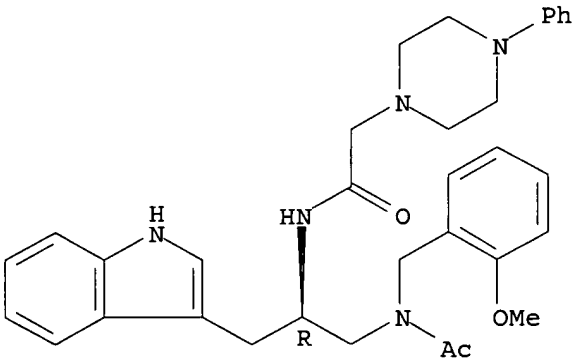
tachykinin NK3 receptor agonist senktide. LY303870 and LY306740 appear to be the most interesting antagonists since they act in a specific and selective manner at the tachykinin NK1 receptor. The difference in the order of potency of the three antagonists to inhibit the hypotension and salivation elicited by substance P could be ascribed to their **pharmacodynamic** features or to the existence of different signal transduction mechanisms or receptor subtypes.

IT **170566-51-5**, LY 303241
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(peripheral effects of three novel non-peptide tachykinin NK1 receptor antagonists in anesthetized rat)

RN 170566-51-5 CA

CN 1-Piperazineacetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]-4-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-51-5**, LY 303241 **170566-84-4**, LY 303870
170567-08-5, LY 306740
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(peripheral effects of three novel non-peptide tachykinin NK1 receptor antagonists in anesthetized rat)

L15 ANSWER 45 OF 65 CA COPYRIGHT 2003 ACS

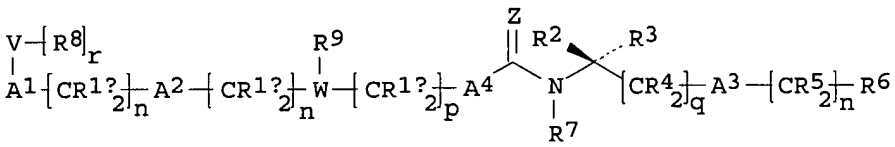
ACCESSION NUMBER:	126:117978 CA
TITLE:	Preparation of heterocycle-containing low molecular peptidyl compounds as inhibitors of farnesyl-protein transferase
INVENTOR(S):	Anthony, Neville J.; Solinsky, Kelly M.; Gomez, Robert P.; Williams, Theresa M.; Bergman, Jeffrey M.; DeSolms, S. Jane; Dinsmore, Christopher J.; MacTough, Suzanne C.
PATENT ASSIGNEE(S):	Merck and Co., Inc., USA; Anthony, Neville J.; Solinsky, Kelly M.; Gomez, Robert P.; Williams, Theresa M.; Bergman, Jeffrey M.; DeSolms, S. Jane; Dinsmore, Christopher J.; MacTough, Suzanne C.
SOURCE:	PCT Int. Appl., 237 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639137	A1	19961212	WO 1996-US8740	19960603
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2223561	AA	19961212	CA 1996-2223561	19960603
AU 9661505	A1	19961224	AU 1996-61505	19960603
AU 708564	B2	19990805		
EP 833633	A1	19980408	EP 1996-919068	19960603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

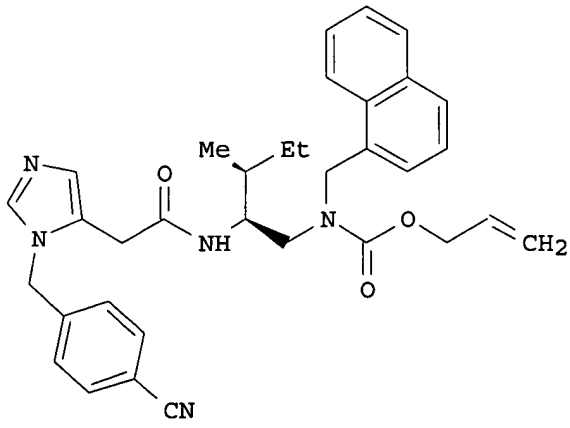
PRIORITY APPLN. INFO.: US 1995-468160 19950606
WO 1996-US8740 19960603

OTHER SOURCE(S): MARPAT 126:117978

GI



I



II

AB The title compds. [I; R1a = H, aryl, heterocycle, etc.; R1b = H, (un)substituted aryl, heterocycle, etc.; R2, R3 = a side chain of a naturally occurring amino acid, (un)substituted C1-20 alkyl, etc.; R4, R5 = H, (un)substituted C1-6 alkyl, aryl, etc.; R6 = H, aryl, C3-10 cycloalkyl, etc.; R7 = H, (un)substituted aryl, heterocyclyl, etc.; R8 = H, (un)substituted aryl, heterocyclyl, etc.; R9 = H, C2-20 alkenyl, C2-20 alkynyl, etc.; A1-A3 = a bond, CH:CH, C.tplbond.C, etc.; A4 = a bond, NR7, S, O; V = H, heterocycle, aryl, etc.; W = heterocycle; Z = O, (R1a)2; n, p, q = 0-4; r = 0-5], which differ from the mono- or dipeptidyl analogs previously described as inhibitors of farnesyl-protein transferase in that they do not have a thiol moiety, were prepd. The lack of the thiol offers

unique advantages in terms of improved **pharmacokinetic** behavior in animals, prevention of thiol-dependent chem. reactions, such as rapid autoxidn. and formation with endogenous thiols, and reduced systemic toxicity. Coupling N-allyloxycarbonyl-N-naphth-1-ylmethyl-2(S)-amino-3(S)-methylpentanamine.HCl with [1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetic acid in the presence of HOBT, Et3N, EDC in DMF afforded the title compd. 2(S),3(S)-II.HCl. In general, compds. I showed IC50 of < 50 .mu.M against human FPTase.

IT **186199-44-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocycle-contg. low mol. peptidyl compds. as inhibitors of farnesyl-protein transferase)

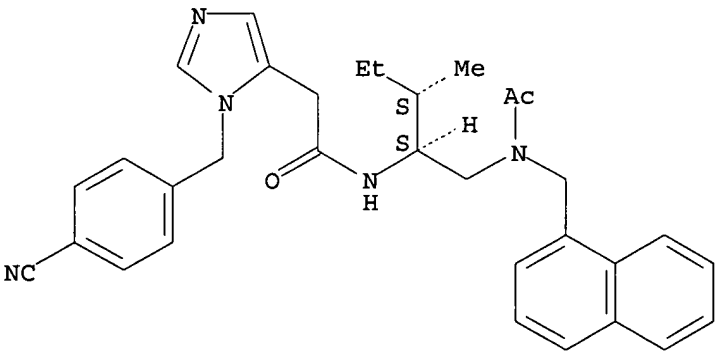
RN 186199-44-0 CA

CN 1H-Imidazole-5-acetamide, N-[(1S,2S)-1-[[acetyl(1-naphthalenylmethyl)amino]methyl]-2-methylbutyl]-1-[(4-cyanophenyl)methyl]-, trifluoroacetate (2:5) (9CI) (CA INDEX NAME)

CM 1

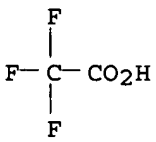
CRN 186199-43-9
CMF C32 H35 N5 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **186199-44-0P 186199-46-2P 186201-10-5P 186201-11-6P 186201-13-8P 186201-14-9P 186201-15-0P 186201-18-3P 186201-19-4P 186201-61-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocycle-contg. low mol. peptidyl compds. as inhibitors of farnesyl-protein transferase)

L15 ANSWER 46 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:99332 CA
TITLE: Use of tachykinin receptors antagonists for the treatment of cold and allergic rhinitis
INVENTOR(S): Gilfillan, Derek James; Iyengar, Smirti; Johnson, Kirk Willis; Mitchell, Malcolm Ian; Phebus, Lee Alan
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 747055	A2	19961211	EP 1996-304170	19960606
EP 747055	A3	19970205		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
WO 9641631	A1	19961227	WO 1996-US8335	19960603
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9659660	A1	19970109	AU 1996-59660	19960603

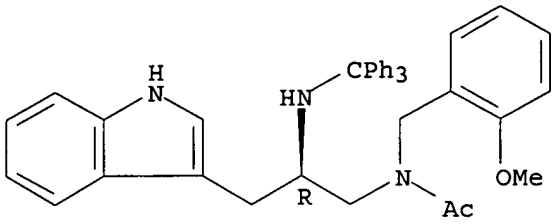
PRIORITY APPLN. INFO.: US 1995-97P P 19950609
WO 1996-US8335 W 19960603

AB Methods are provided for the treatment or amelioration of the symptoms of the common cold or allergic rhinitis. The methods comprise administering to a mammal in need thereof a compd. having activity as a tachykinin receptor antagonist. Prepn. of selected tachykinin antagonists, e.g. (R)-2-[N-(2-((4-cyclohexyl)piperazin-1-yl)acetyl)amino]-3-(1H-indol-3-yl)-1-[N-(2-methoxybenzyl)acetylamino]propane, is included. NK-1 and NK-2 receptor binding assays are described, as are active-ingredient formulations.

IT **175460-97-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; tachykinin receptors antagonists, prepn., and **pharmaceutical** compns. for the treatment of cold and allergic rhinitis)

RN 175460-97-6 CA
CN Acetamide, N-[(2R)-3-(1H-indol-3-yl)-2-[(triphenylmethyl)amino]propyl]-N-[(2-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **175460-97-6P 175460-98-7P 175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; tachykinin receptors antagonists, prepn., and **pharmaceutical** compns. for the treatment of cold and allergic rhinitis)

IT **167678-33-3P 170566-84-4P 170567-08-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin receptors antagonists, prepn., and **pharmaceutical** compns. for the treatment of cold and allergic rhinitis)

L15 ANSWER 47 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:99331 CA
TITLE: Use of tachykinin antagonists in combination with serotonin agonists or serotonin reuptake inhibitors for the manufacture of a medicament for the treatment of common cold or allergic rhinitis
INVENTOR(S): Johnson, Kirk Willis; Phebus, Lee Alan
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

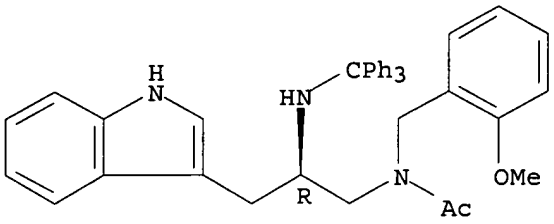
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 747049	A1	19961211	EP 1996-304183	19960606
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
WO 9641633	A1	19961227	WO 1996-US8336	19960603
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9659661	A1	19970109	AU 1996-59661	19960603

PRIORITY APPLN. INFO.: US 1995-74P P 19950608
WO 1996-US8336 W 19960603

AB Methods are provided for the treatment or amelioration of the symptoms of the common cold or allergic rhinitis which comprise administering to a mammal in need thereof a combination of a tachykinin receptor antagonist and either a serotonin agonist or a selective serotonin reuptake inhibitor. The administration may be concurrent or sequential, with either of the two activities being administered first. Compd. prepn. and active-ingredient formulations are included.

IT **175460-97-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; tachykinin antagonist combination with serotonin agonist or serotonin reuptake inhibitor for treatment of common cold or allergic rhinitis, compd. prepn., and **pharmaceutical** formulations)
RN 175460-97-6 CA
CN Acetamide, N-[(2R)-3-(1H-indol-3-yl)-2-[(triphenylmethyl)amino]propyl]-N-[(2-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **175460-97-6P 175460-98-7P 175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; tachykinin antagonist combination with serotonin agonist or serotonin reuptake inhibitor for treatment of common cold or allergic rhinitis, compd. prepn., and **pharmaceutical** formulations)
IT **167678-33-3P 170566-84-4P 170567-08-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin antagonist combination with serotonin agonist or serotonin reuptake inhibitor for treatment of common cold or allergic rhinitis, compd. prepn., and **pharmaceutical** formulations)

L15 ANSWER 48 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:339038 CA
TITLE: A tachykinin receptor antagonist and a serotonin agonist for treating or preventing pain or nociception
INVENTOR(S): Johnson, Kirk W.; Phebus, Lee A.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629074	A1	19960926	WO 1996-US4198	19960320

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML

AU 9655289 A1 19961008 AU 1996-55289 19960320
PRIORITY APPLN. INFO.: US 1995-408238 19950322
WO 1996-US4198 19960320
OTHER SOURCE(S): MARPAT 125:339038

AB This invention provides methods for the treatment or prevention of pain or nociception which comprises administering to a mammal in need thereof a combination of a tachykinin receptor antagonist and either a serotonin agonist or a selective serotonin reuptake inhibitor. This administration may be concurrent or sequential, with either of the two activities being administered first. Synthesis of several tachykinin receptor antagonists, such as (R)-2-[N-(2-((4-cyclohexyl)piperazin-1-yl)acetyl)amino]-3-(1H-indol-3-yl)-1-[N-(2-methoxybenzyl)acetylamino]propane, is presented and various **pharmaceutical** formulations were proposed.

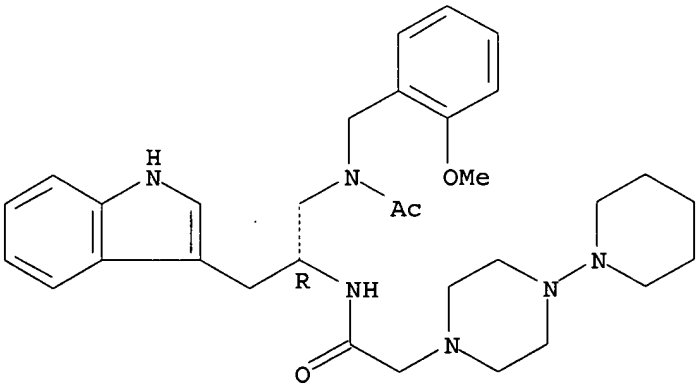
IT **183231-16-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(combination of serotonin agonist and tachykinin receptor antagonist for preventing or treating pain)

RN 183231-16-5 CA
CN 1-Piperazineacetamide, N-[2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]-4-(1-piperidinyl)-, (R)-, ethanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

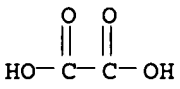
CRN 183231-13-2
CMF C32 H44 N6 O3

Absolute stereochemistry.



CM 2

CRN 144-62-7
CMF C2 H2 O4



IT **183231-16-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(combination of serotonin agonist and tachykinin receptor antagonist for preventing or treating pain)

IT **170567-08-5P 183231-13-2P 183231-17-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combination of serotonin agonist and tachykinin receptor antagonist for preventing or treating pain)

IT **175460-97-6P 175460-98-7P 175460-99-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(combination of serotonin agonist and tachykinin receptor antagonist for preventing or treating pain)

L15 ANSWER 49 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:257222 CA
TITLE: Methods of treating or preventing psychiatric disorders
INVENTOR(S): Johnson, Kirk W.; Phebus, Lee A.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9624353	A1	19960815	WO 1996-US1737	19960208
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
AU 9649187	A1	19960827	AU 1996-49187	19960208

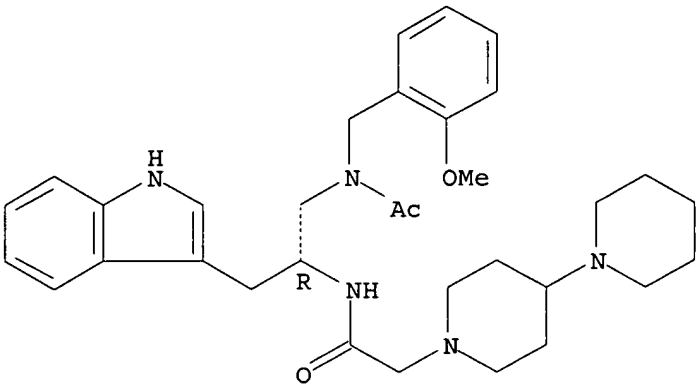
PRIORITY APPLN. INFO.: US 1995-387056 19950210
WO 1996-US1737 19960208

AB This invention provides methods for the treatment or prevention of psychiatric disorders which comprises administering to a mammal a combination of a tachykinin receptor antagonist and either a serotonin agonist or a selective serotonin reuptake inhibitor. This administration may be concurrent or sequential, with either of the 2 activities being administered first. The psychiatric disorders which may be treated by the methods of the invention include panic disorder, panic attack, depression, anxiety, obsessive-compulsive disorder, post-traumatic stress disorder, borderline personality disorder, etc. Thus, (R)-2-[N-(2-((4-cyclohexyl)piperazin-1-yl)acetyl)amino]-3-(1H-indol-3-yl)-1-[N-(2-methoxybenzyl)acetylamino]propane was prepd. by a series of steps starting from D-tryptophan. Hard gelatin capsules were each prepd. contg. active ingredient(s) 30.0, starch 305.0, and Mg stearate 5.0 mg. Radioreceptor binding assay studies performed by using the active ingredients on NK-1 or NK-2 receptors showed that the compds. were effective antagonists of these receptors.

IT **170566-84-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of treating or preventing psychiatric disorders)
RN 170566-84-4 CA
CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170566-84-4P 170567-08-5P 182317-87-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of treating or preventing psychiatric disorders)
IT **175460-97-6P 175460-98-7P 175460-99-8P 182317-88-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(methods of treating or preventing psychiatric disorders)

L15 ANSWER 50 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:67748 CA
TITLE: Methods of treating migraine with a tachykinin antagonist and a serotonin agonist
INVENTOR(S): Cohen, Marlene Lois; Johnson, Kirk Willis; Phebus, Lee Alan
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611000	A1	19960418	WO 1995-US13087	19951004

W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN
RW: KE, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5744482	A	19980428	US 1994-318391	19941005
ZA 9508173	A	19970401	ZA 1995-8173	19950928
EP 710479	A1	19960508	EP 1995-307000	19951003
EP 710479	B1	19990107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 175347	E	19990115	AT 1995-307000	19951003
ES 2125567	T3	19990301	ES 1995-307000	19951003
AU 9641301	A1	19960502	AU 1996-41301	19951004
PRIORITY APPLN. INFO.:			US 1994-318391 A	19941005
			WO 1995-US13087 W	19951004

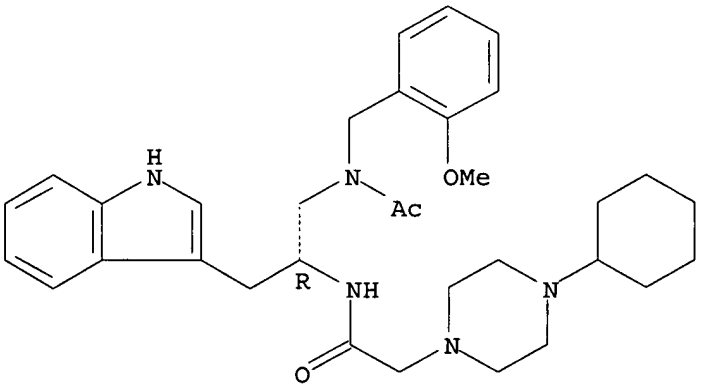
AB This invention provides methods for the treatment or prevention of migraines which comprises administering to a mammal in need thereof a combination of a tachykinin receptor antagonist and a serotonin agonist. This administration may be concurrent or sequential, with either of the two activities being administered first.

IT **170567-08-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(methods of treating migraine with a tachykinin antagonist and a serotonin agonist)

RN 170567-08-5 CA

CN 1-Piperazineacetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]-4-cyclohexyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **170567-08-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(methods of treating migraine with a tachykinin antagonist and a serotonin agonist)

IT **170566-84-4**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(methods of treating migraine with a tachykinin antagonist and a serotonin agonist)

L15 ANSWER 51 OF 65 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 124:343300 CA

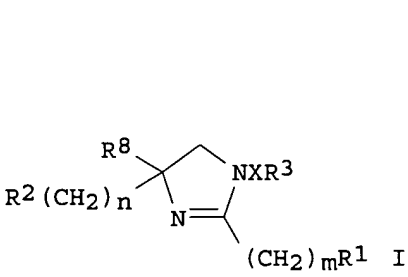
TITLE: Preparation of imidazoline derivatives as tachykinin receptor antagonists

INVENTOR(S): Hipskind, Philip Arthur; Howbert, James Jeffry; Muehl,

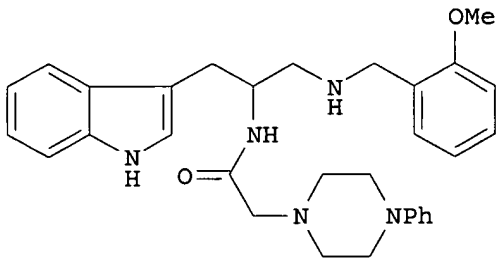
Brian Stephen
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Can. Pat. Appl., 61 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2151113	AA	19951211	CA 1995-2151113	19950606
US 6175013	B1	20010116	US 1994-257966	19940610
EP 699665	A1	19960306	EP 1995-303820	19950605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07330736	A2	19951219	JP 1995-141893	19950608

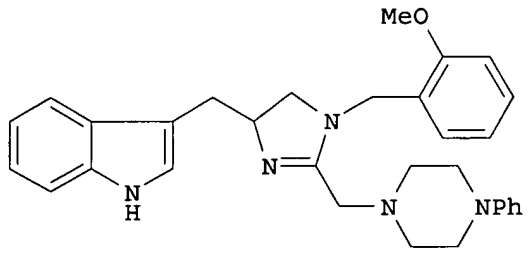
PRIORITY APPLN. INFO.: US 1994-257966 A 19940610
OTHER SOURCE(S): MARPAT 124:343300
GI



I



II

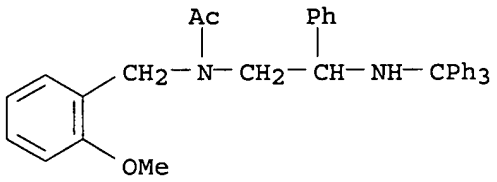


III

AB The invention provides novel substituted 2-imidazolines I [X = (CHR4)p(CHR6)q; m, n, p, q = 0, 1; R1 = H, (un)substituted trityl, Ph, Ph2CH, PhO, PhS, piperazinyl, piperidinyl, indolyl, amino, leaving group, NHCH2R5, etc.; R2 = (un)substituted Ph, 2- or 3-indolyl or -indolinyl, benzothienyl, benzofuranyl, naphthyl; R3 = (un)substituted Ph, phenylalkylidene, cycloalkyl, alkyl, H, alkenyl, cycloalkenyl; R4, R6 = H, alkyl; R5 = pyridyl, anilinoalkylidenyl, anilinocarbonyl] and their salts and solvates. The compds. are useful in the treatment or prevention of a variety of physiol. disorders assocd. with an excess of tachykinins. For example, Boc-Trp-OH was converted in 4 steps to intermediate II, which was cyclized in 83% yield in refluxing 1,2-Cl2C6H4 to give title compd. III. In NK-1 and NK-2 receptor binding assays, III had IC50 values of 0.12 and 0.47 .mu.M, resp.
IT **170568-08-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

RN 170568-08-8 CA
CN Acetamide, N-[(2-methoxyphenyl)methyl]-N-[2-phenyl-2-[(triphenylmethyl)amino]ethyl]- (9CI) (CA INDEX NAME)



IT **170568-08-8P 170568-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

L15 ANSWER 52 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:290273 CA
TITLE: Preparation of peptide analogs as inhibitors of interleukin-1 beta converting enzyme (ICE)
INVENTOR(S): Bemis, Guy W.; Golec, Julian M. C.; Lauffer, David J.; Mullican, Michael D.; Murcko, Mark A.; Livingston, David J.
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorp., USA
SOURCE: PCT Int. Appl., 374 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

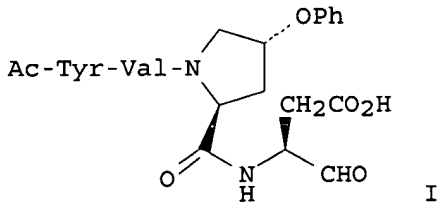
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9535308	A1	19951228	WO 1995-US7617	19950616
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5756466	A	19980526	US 1994-261452	19940617
US 5656627	A	19970812	US 1995-405581	19950317
US 5847135	A	19981208	US 1995-440898	19950525
AU 9529446	A1	19960115	AU 1995-29446	19950616
AU 709114	B2	19990819		
EP 784628	A1	19970723	EP 1995-925257	19950616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9508051	A	19971021	BR 1995-8051	19950616
JP 10504285	T2	19980428	JP 1996-502478	19950616
NO 9605365	A	19970217	NO 1996-5365	19961213
FI 9605036	A	19970214	FI 1996-5036	19961216
US 6420522	B1	20020716	US 1999-430822	19991029

PRIORITY APPLN. INFO.: US 1994-261452 A 19940617

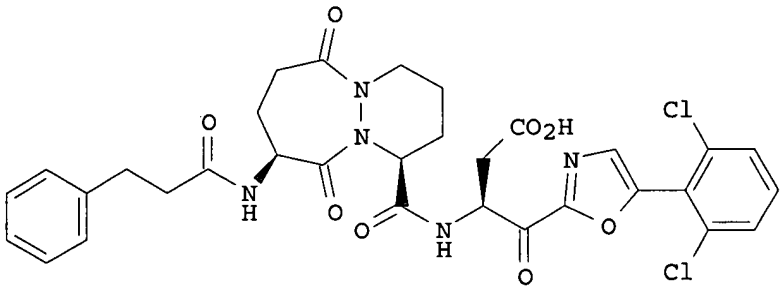
US 1995-405581 A 19950317
US 1995-440898 A 19950525
US 1995-465216 A3 19950605
WO 1995-US7617 W 19950616

OTHER SOURCE(S): MARPAT 124:290273

GI



I



II

AB Novel classes of compds. are prepd., which are characterized by specific structural and physicochem. features comprising (a) a first and a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE selected from the carbonyl O and the amide NH group of Arg-341 Ser-339, (b) a first and a second moderately hydrophobic moiety, said moieties each being capable of assocg. with a sep. binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected form the P2, P3, P4, and P' binding pockets, and (c) an electroneg. moiety comprising .gtoreq.1 electroneg. atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being capable of forming .gtoreq.1 hydrogen bonds or salts bridges with residues in the P1 binding pocket of ICE. These compds. and **pharmaceutical** compns. of this invention are particularly well suited for inhibiting ICE activity and consequently may be advantageously used as agents against interleukin-1 mediated diseases, including inflammatory diseases, autoimmune diseases and neurodegenerative diseases. Thus, etherification of Me N-tert-butoxycarbonyl-cis-4-hydroxyprolinate with phenol using Ph3P and di-Et azodicarboxylate in THF to Me N-tert-butoxycarbonyl-cis-4-phenoxyprolinate followed by deprotection with HCl in EtOAc to Me 4-phenoxyprolinate hydrochloride and condensation with Ac-Tyr-Val-OH using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, HOBT, and diisopropylethylamine in DMF gave Me N-acetyl-L-tyrosinyl-L-valyl-(4-phenoxy)prolinate. Sapon. of the latter peptide ester with LiOH in aq. THF to N-acetyl-L-tyrosinyl-L-valyl-(phenoxy)proline followed by condensation with N-allyloxycarbonyl-4-amino-5-benzyloxy-2-oxotetrahydrofuran gave N-[N-acetyl-L-tyrosinyl-L-valyl-(4-phenoxy)prolinyl]-4-amino-5-benzyloxy-2-oxotetrahydrofuran (1:1 diastereomer mixt.), which underwent hydrogenolysis over Pd(OH)2 in MeOH under H atm. to give the title compd. (I). In a IL-1.beta. assay with a mixed population of human peripheral blood mononuclear cells or enriched

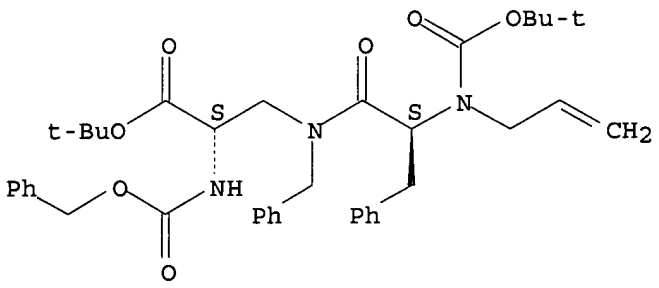
adherent mononuclear cells, I in vitro showed IC50 of 2.6 and 0.25 .mu.M for inhibiting the processing of pre-IL-1.beta. by ICE.

IT **175211-56-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptide analogs as inhibitors of interleukin-1 beta converting enzyme for treating inflammatory, autoimmune and neurodegenerative diseases)

RN 175211-56-0 CA

CN .beta.-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-N-2-propenyl-L-phenylalanyl-2-[[(phenylmethoxy)carbonyl]amino]-N-(phenylmethyl)-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **175211-56-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptide analogs as inhibitors of interleukin-1 beta converting enzyme for treating inflammatory, autoimmune and neurodegenerative diseases)

L15 ANSWER 53 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:21680 CA
TITLE: **Pharmacological** characterization of LY303870: a novel, potent and selective nonpeptide substance P (neurokinin-1) receptor antagonist
AUTHOR(S): Gitter, Bruce D.; Bruns, Robert F.; Howbert, J. Jeffry; Waters, Diane C.; Threlkeld, Penny G.; Cox, Laura M.; Nixon, James A.; Lobb, Karen L.; Mason, Norman R.; et al.
CORPORATE SOURCE: Research Divisions, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis ld R., IN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1995), 275(2), 737-44
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB LY303870 [(R)-1-[N-(2-methoxybenzyl)acetylamino]-3-(1H-indol-3-yl)-2-[N-(2-(4-(piperidin-1-yl)piperidin-1-yl)acetyl)amino]-propane] is a new, potent and selective nonpeptide neurokinin-1 (NK-1) receptor antagonist. LY303870 bound selectively and with high affinity to human peripheral (Ki = 0.15 nM) and central (Ki = 0.10 nM) NK-1 receptors. LY303870 inhibited [125I]substance P (SP) binding to guinea pig brain homogenates with similar affinity; however, it had approx. 50-fold lesser affinity for rat NK-1 sites. The less active enantiomer, LY306155 {(S)-1-[N-(2-methoxybenzyl)acetylamino]-3-(1H-indol-3-yl)-2-[N-(2-(4-(piperidin-1-

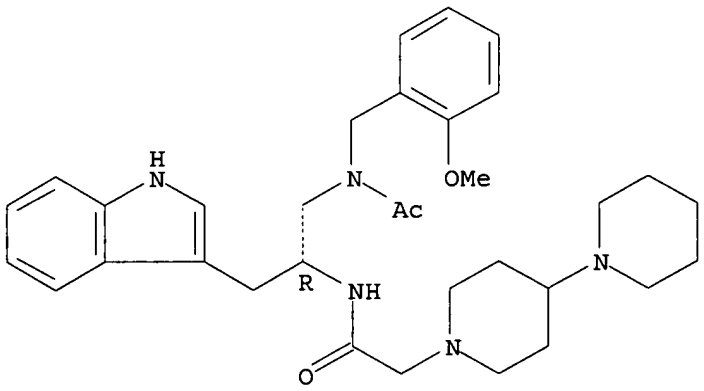
yl)piperidin-1-yl)acetyl)amino]-propane}, was 1,000- to 15,000-fold less potent in all the species examd. LY303870 antagonized in vitro NK-1 receptor effects as demonstrated by blockade of SP-stimulated phosphoinositide turnover in UC=11 MG human astrocytoma cells (Ki = 1.4 nM) and interleukin-6 secretion from U-373 MG human astrocytoma cells (Ki = 5 nM). In addn., LY303870 inhibited SP-induced rabbit vena cava contractions (pA2 = 9.4) with high (50,000-fold) selectivity vs. NK-2 or NK-3 receptor-mediated responses. In vivo, LY303870 inhibited [Sar9,-Met(O2)11]-SP induced guinea pig bronchoconstriction (ED50 = 75 .mu.g/kg i.v.) and pulmonary microvascular leakage in the bronchi (ED50 = 12.8 .mu.g/kg i.v.) and trachea (ED50 = 18.5 .mu.g/kg i.v.). Therefore, LY303870 is a potent and selective NK-1 receptor antagonist in vitro and in vivo. The use of LY303870 will facilitate a better understanding of NK-1 receptors in physiol. processes.

IT **170566-84-4**, LY 303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**pharmacol**. characterization of neurokinin-1 receptor antagonist LY303870)

RN 170566-84-4 CA

CN [1,4'-Bipiperidine]-1'-acetamide, N-[(1R)-2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-(1H-indol-3-ylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



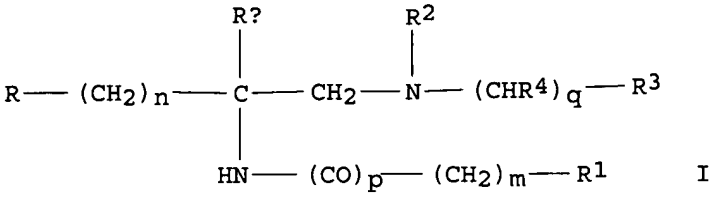
IT **170566-84-4**, LY 303870
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**pharmacol**. characterization of neurokinin-1 receptor antagonist LY303870)

L15 ANSWER 54 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 123:339728 CA
TITLE: Non-peptide tachykinin receptor antagonists
INVENTOR(S): Cho, Sung-Yong Stephen; Crowell, Thomas Alan; Gitter, Bruce Donald; Hipskind, Philip Arthur; Howbert, James Jeffry; Krushinski, Joseph Herman, Jr.; Lobb, Karen Lynn; Muehl, Brian Stephen; Nixon, James Arthur
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2

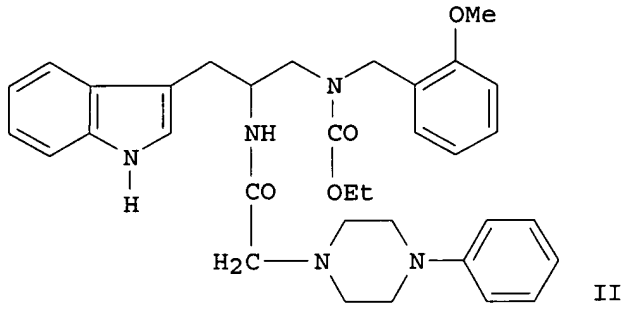
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514017	A1	19950526	WO 1994-US13222	19941116
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6403577	B1	20020611	US 1993-153847	19931117
ZA 9408926	A	19960510	ZA 1994-8926	19941110
CA 2176735	AA	19950526	CA 1994-2176735	19941116
AU 9510988	A1	19950606	AU 1995-10988	19941116
EP 729468	A1	19960904	EP 1995-901928	19941116
EP 729468	B1	20030115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1141043	A	19970122	CN 1994-194790	19941116
CN 1078889	B	20020206		
JP 09505304	T2	19970527	JP 1994-514583	19941116
HU 76269	A2	19970728	HU 1996-1304	19941116
BR 9408063	A	19990824	BR 1994-8063	19941116
RU 2140921	C1	19991110	RU 1996-113087	19941116
TW 412512	B	20001121	TW 1994-83110634	19941116
PL 180150	B1	20001229	PL 1994-331233	19941116
US 5670499	A	19970923	US 1995-462415	19950605
US 5684033	A	19971104	US 1995-463874	19950605
FI 9602074	A	19960515	FI 1996-2074	19960515
NO 9602012	A	19960708	NO 1996-2012	19960515
AU 9897255	A1	19990225	AU 1998-97255	19981221
AU 721935	B2	20000720		

PRIORITY APPLN. INFO.: US 1993-153847 A 19931117
AU 1995-10988 A3 19941116
WO 1994-US13222 W 19941116
OTHER SOURCE(S): CASREACT 123:339728; MARPAT 123:339728
GI



I



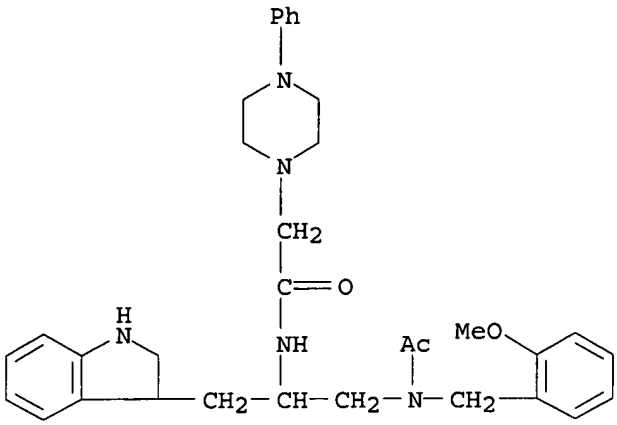
II

AB The invention provides a novel series of non-peptide compds. I [m, n, p = 0, 1; q = 0, 1, 2; R = (un)substituted Ph, 2- or 3-indolyl or -indolinyl, benzothienyl, benzofuranyl, or naphthyl; R1 = (un)substituted trityl, Ph, PhO, PhS, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, indolyl, amino, H, leaving group, etc.; R2 = H, alkyl, arylsulfonyl, alkylsulfonyl, carboxyalkyl, alkoxycarbonylalkyl, acyl; R3 = H, (un)substituted Ph, phenylalkyl, (cyclo)alk(en)yl, naphthyl; R4 = H, alkyl; R3 .noteq. H or alk(en)yl if R1 = H or halo] and their salts and solvates. The compds. are useful in the treatment or prevention of physiol. disorders assocd. with excess tachykinins. This invention also provides methods of treatment and **pharmaceutical** formulations employing I. Over 170 examples were prepd. and tested for biol. activity, and 11 formulations are described. For instance, activation of N-(tert-butoxycarbonyl)tryptophan with carbonyldiimidazole (CDI) and reaction with 2-MeOC6H4CH2NH2 gave 80.8% of the corresponding 2-methoxybenzylamide, which was deprotected (94.2%), reduced at the amide carbonyl with BH3.SMe2, coupled with Na 2-(4-phenylpiperazin-1-yl)acetic acid using CDI, and N-acylated with ClCO2Et and Et3N, to give title compd. II. This compd. had IC50 values of 1.7 and 1000 nM for binding to human NK-1 and NK-2 receptors, resp., in cultured cell assays.

IT **170567-77-8P**
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(byproduct; prepn. of non-peptide tachykinin receptor antagonists)

RN 170567-77-8 CA

CN 1-Piperazineacetamide, N-[2-[acetyl[(2-methoxyphenyl)methyl]amino]-1-[(2,3-dihydro-1H-indol-3-yl)methyl]ethyl]-4-phenyl- (9CI) (CA INDEX NAME)



IT **170567-77-8P**
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(byproduct; prepn. of non-peptide tachykinin receptor antagonists)

IT **170568-21-5P 170568-22-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of non-peptide tachykinin receptor antagonists)

IT **170566-45-7P 170566-46-8P 170566-47-9P**
170566-48-0P 170566-49-1P 170566-50-4P
170566-51-5P 170566-52-6P 170566-53-7P
170566-54-8P 170566-55-9P 170566-56-0P
170566-57-1P 170566-58-2P 170566-59-3P
170566-63-9P 170566-64-0P 170566-65-1P
170566-66-2P 170566-67-3P 170566-68-4P
170566-69-5P 170566-79-7P 170566-80-0P
170566-81-1P 170566-82-2P 170566-83-3P
170566-84-4P 170566-85-5P 170566-88-8P
170566-89-9P 170566-90-2P 170566-91-3P
170566-92-4P 170566-93-5P 170566-94-6P
170566-95-7P 170566-96-8P 170566-97-9P
170566-98-0P 170566-99-1P 170567-00-7P
170567-01-8P 170567-02-9P 170567-03-0P
170567-04-1P 170567-05-2P 170567-06-3P
170567-07-4P 170567-08-5P 170567-09-6P
170567-10-9P 170567-11-0P 170567-12-1P
170567-13-2P 170567-14-3P 170567-15-4P
170567-16-5P 170567-17-6P 170567-18-7P
170567-19-8P 170567-20-1P 170567-21-2P
170567-22-3P 170567-23-4P 170567-24-5P
170567-25-6P 170567-26-7P 170567-27-8P
170567-28-9P 170567-29-0P 170567-30-3P
170567-31-4P 170567-32-5P 170567-33-6P
170567-36-9P 170567-37-0P 170567-39-2P
170567-40-5P 170567-41-6P 170567-42-7P
170567-46-1P 170567-47-2P 170567-48-3P
170567-49-4P 170567-50-7P 170567-51-8P
170567-52-9P 170567-57-4P 170567-58-5P
170567-59-6P 170567-60-9P 170567-61-0P
170567-62-1P 170567-63-2P 170567-64-3P
170567-71-2P 170567-72-3P 170567-73-4P
170567-74-5P 170567-75-6P 170567-76-7P

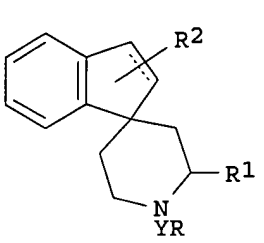
170567-77-8P 170567-78-9P 170567-79-0P
170567-80-3P 170567-81-4P 170567-82-5P
170567-92-7P 170567-93-8P 170567-94-9P
170567-95-0P 170568-08-8P 170568-09-9P
170568-10-2P 170568-25-9P 170568-26-0P
170568-27-1P 170568-28-2P 170568-29-3P
170568-30-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of non-peptide tachykinin receptor antagonists)

IT **170568-23-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of non-peptide tachykinin receptor antagonists)

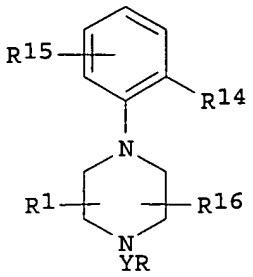
L15 ANSWER 55 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 123:330860 CA
TITLE: Tocolytic oxytocin receptor antagonists
INVENTOR(S): Bock, Mark G.; Evans, Ben E.; Culberson, J. Christopher; Gilbert, Kevin F.; Rittle, Kenneth E.; Williams, Peter D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9525443	A1	19950928	WO 1995-US3738	19950323
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5464788	A	19951107	US 1994-217270	19940324
CA 2186129	AA	19950928	CA 1995-2186129	19950323
AU 9521952	A1	19951009	AU 1995-21952	19950323
AU 686792	B2	19980212		
EP 751773	A1	19970108	EP 1995-914875	19950323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09512521	T2	19971216	JP 1995-524838	19950323
US 5756504	A	19980526	US 1996-718415	19960923

PRIORITY APPLN. INFO.: US 1994-217270 19940324
WO 1995-US3738 19950323
OTHER SOURCE(S): MARPAT 123:330860
GI



I



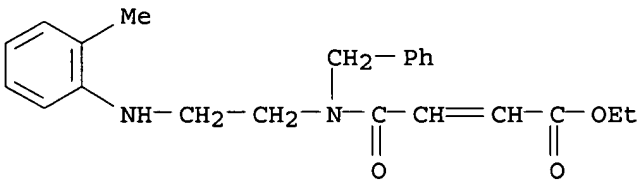
II

AB Spiroindenepiperidine derivs. I [R1 = H, C1-5 alkyl, CN, CO2H, Ph, etc.; R2 = H, PhCH2, C3-8 cycloalkyl, C1-5 alkyl; Y = CO2, C(O)NR2, C(:NR2), SO2, C(O)(CH2)n, (CH2)p, (CH2)pC(O); R = (tetrahydro)naphthyl, (substituted) cyclohexyl, (substituted) Ph, heterocyclyl; bond in cyclopentane ring is single or double; n = 0-3; p = 1-3] and phenylpiperazine derivs. II (Y, R, R1 as above; R14, R15 = H, C1-5 alkyl, C1-5 alkoxy, halo, NO2, CN; R16 = H, :O) and their **pharmaceutically** acceptable salts and esters are useful as oxytocin and vasopressin receptor antagonists for treatment of preterm labor and dysmenorrhea and for stopping labor prior to cesarean delivery. Thus, 1-[2-methoxy-4-[1-[2-(N-cyclopropylamino)ethylsulfonyl]-4-piperidyloxy]phenylacetyl]-4-(2-methylphenyl)piperazine-2-carboxamide (III) was prepd. in 11 steps from 4-hydroxypiperidine, Me 2,4-dihydroxybenzoate, 2-benzylaminoethanol, o-toluidine, 2,3-dibromopropionamide, and cyclopropylamine. III competed with 1 nM oxytocin-3H for binding to rat uterine tissue with an IC50 of 20 nM.

IT **170930-07-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tocolytic oxytocin receptor antagonists)

RN 170930-07-1 CA

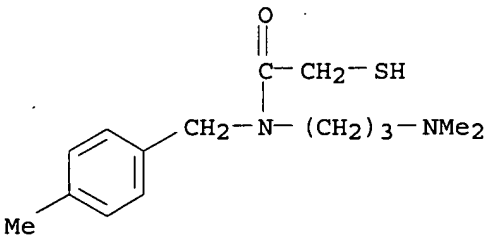
CN 2-Butenoic acid, 4-[[2-[(2-methylphenyl)amino]ethyl](phenylmethyl)amino]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



IT **170930-07-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tocolytic oxytocin receptor antagonists)

L15 ANSWER 56 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 122:230112 CA
TITLE: Synthesis and structure-activity relationships of 2-(substituted)-3-[3-(N,N-dimethylamino)propyl]-1,3-thiazolidin-4-ones and related analogues acting as H1-histamine antagonists
AUTHOR(S): Diurno, M. Vittoria; Greco, Giovanni; Mazzoni, Orazio; Novellino, Ettore; Calignano, Antonio; La Rana,

Giovanna; Barbieri, Antonio; Bolognese, Adele
CORPORATE SOURCE: Dipartimento di Chimica Farmaceutica e Tossicologica, Universita di Napoli "Federico II", Naples, 80131, Italy
SOURCE: Medicinal Chemistry Research (1994), 4(9), 578-87
CODEN: MCREEB; ISSN: 1054-2523
PUBLISHER: Birkhaeuser
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Analogs of 2-(4-methylphenyl)-3-[3-(N,N-dimethylamino)propyl]-1,3-thiazolidin-4-one, recently reported as a new H1-histamine antagonist, have been synthesized and tested for their H1-antihistaminic and sedative activities. Structural modifications have specifically involved the 2-aryl-1,3-thiazolidin-4-one moiety with the aim to derive useful structure-activity relationships and hoping to detect more potent compds. The results of the present study have led to a more precise definition of some **pharmacophoric** elements. Moreover, among the newly synthesized set of analogs, 2-(4-methylphenyl)-5-methyl-3-[3-(N,N-dimethylamino)propyl]-1,3-thiazolidin-4-one (as 1 of a set of 2 racemic mixts.) was found to be slightly more potent than mepyramine on the H1-receptor and, at the same time, about four times less sedative than the ref. **drug**.
IT **162321-78-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and structure-activity relationships of (dimethylamino)propylthiazolidinones and related analogs acting as H1-histamine antagonists)
RN 162321-78-0 CA
CN Acetamide, N-[3-(dimethylamino)propyl]-2-mercapto-N-[(4-methylphenyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

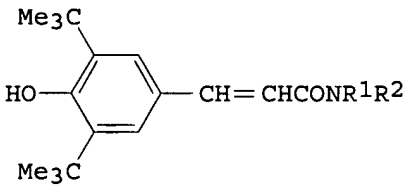
IT **162321-78-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and structure-activity relationships of (dimethylamino)propylthiazolidinones and related analogs acting as H1-histamine antagonists)

L15 ANSWER 57 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 115:28908 CA
TITLE: Preparation of cinnamamide derivatives as antihyperlipidemics

INVENTOR(S): Fuse, Yoshihide; Fujii, Kenji; Kameyama, Keiji; Kawabe, Taizo; Miwa, Toshiaki; Katsumi, Ikuo
PATENT ASSIGNEE(S): Kanegafuchi Chemical Industry Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 407200	A1	19910109	EP 1990-307375	19900705
EP 407200	B1	19940601		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
CA 2020437	AA	19910106	CA 1990-2020437	19900705
JP 03275657	A2	19911206	JP 1990-179138	19900705
US 5294643	A	19940315	US 1990-548121	19900705
US 5294624	A	19940315	US 1992-914298	19920715
US 5352677	A	19941004	US 1992-914753	19920715

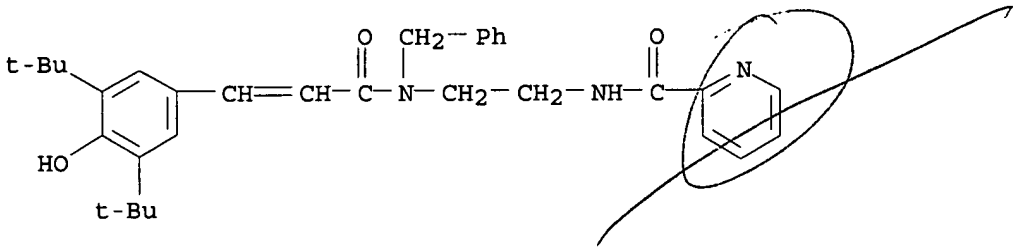
PRIORITY APPLN. INFO.: JP 1989-174820 19890705
JP 1989-174821 19890705
JP 1989-174822 19890705
JP 1990-9528 19900118
JP 1990-9529 19900118
JP 1990-9530 19900118
US 1990-548121 19900705
OTHER SOURCE(S): MARPAT 115:28908
GI



I

AB Title compds. I [R1 = H, C1-8 alkyl, carboxyalkyl, alkoxyalkyl, alkylamino, (phenylalkyl)amino, substituted piperazinyl, alkylimidazolyl, [(thiazolylamino)carbonyl]alkyl, etc.; R2 = H, C1-5 alkyl, Ph(CH2)n, n = 1-3; R1R2N = (substituted) heterocyclyl], are prepd. 3,5,4-(Me3C)2(HO)C6H2CH:CHCO2H and PhCH2NH2 were dissolved in CH2Cl2, then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide-HCl was added, and the mixt. reacted for 2 h at room temp., the reaction mixt. washed with H2O and concd. under reduced pressure to give after chromatog. I (R1 = PhCH2, R2 = H) (II). In rats, II at 10 mg/kg-day decreased 30% cholesterol level. Addnl. 93 I compds. were prepd. and showed excellent antihyperlipidemic efficacy. **Pharmaceutical** formulations of I were given.
IT **134502-69-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antihyperlipidemic)
RN 134502-69-5 CA

CN 2-Pyridinecarboxamide, N-[2-[[3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-1-oxo-2-propenyl](phenylmethyl)amino]ethyl]- (9CI) (CA INDEX NAME)



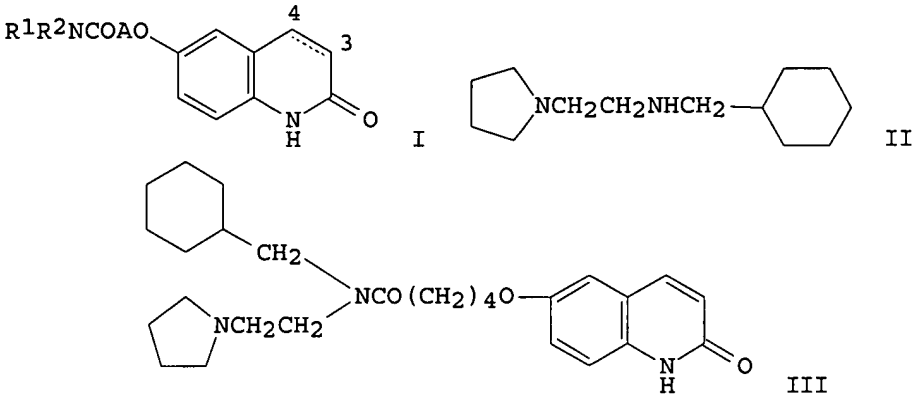
IT **134502-69-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antihyperlipidemic)

L15 ANSWER 58 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 114:6304 CA
TITLE: Preparation of carbostyril derivatives and their **pharmaceutical** compositions as blood platelet aggregation inhibitors
INVENTOR(S): Nishi, Takao; Komatsu, Makoto; Koga, Yasuo; Shu, Yoshio; Tamura, Katsumi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 260 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8910919	A1	19891116	WO 1989-JP464	19890502
W: DK, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
JP 02049768	A2	19900220	JP 1989-109466	19890428
JP 2753622	B2	19980520		
EP 450066	A1	19911009	EP 1989-905166	19890502
EP 450066	B1	19960911		
R: CH, DE, FR, GB, IT, LI, NL, SE				
DK 8906722	A	19900220	DK 1989-6722	19891229
KR 125919	B1	19971226	KR 1989-72502	19891229
US 5227381	A	19930713	US 1992-929097	19920813
US 5401740	A	19950328	US 1994-273624	19940712

PRIORITY APPLN. INFO.: JP 1988-109534 A 19880502
WO 1989-JP464 W 19890502
US 1989-449849 B1 19891227
US 1992-929097 A3 19920813
US 1993-44663 B1 19930409

OTHER SOURCE(S): MARPAT 114:6304
GI

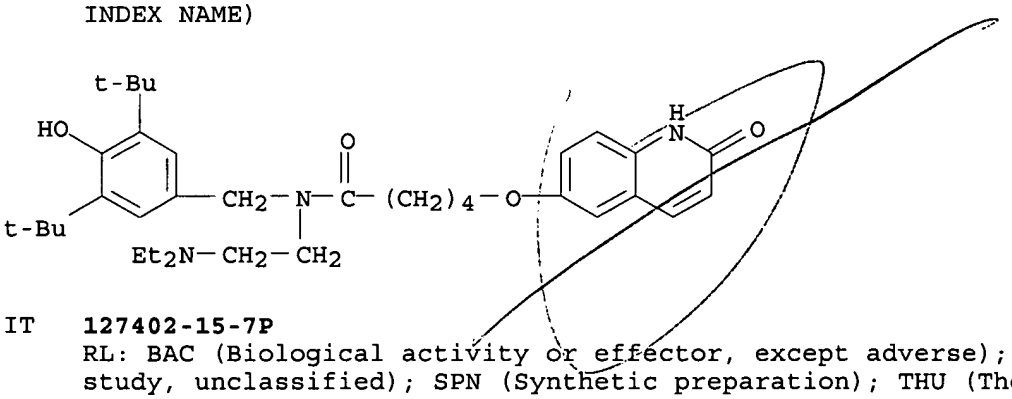


AB Carbostyril derivs. [I; R1 = cycloalkyl, cycloalkylalkyl, aralkyl, alkylpiperidylalkyl, etc.; R2 = (substituted) heterocyclylalkyl, (tetrahydropyranylthio)alkyl, pyridylthioalkyl, (substituted) alkyl; A = alkylene; 3,4-satd. or unsatd.] are prepd. DBU (1.40 g) was added to a suspension of 2.00 g 6-(4-carboxybutoxy)carbostyril in CHCl3 with stirring at room temp., 1.05 g ClCO2CHMe2 was added under cooling, followed by 1.61 g amine II with stirring at room temp. to give 1.00 g carbostyril deriv. II. Similarly prepd. was 129 addnl. I which showed IC50 of 0.071-7.0 .mu.M against collagen-induced platelet aggregation. Tablet, capsule, and injection formulations were given.

IT **127402-15-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as blood platelet aggregation inhibitor)

RN 127402-15-7 CA

CN Pentanamide, N-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methyl]-N-[2-(diethylamino)ethyl]-5-[(1,2-dihydro-2-oxo-6-quinolinyl)oxy]- (9CI) (CA INDEX NAME)



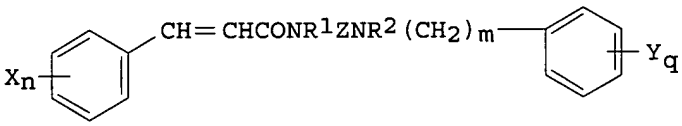
IT **127402-15-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as blood platelet aggregation inhibitor)

L15 ANSWER 59 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 113:190946 CA
TITLE: Preparation of cinnamamide derivatives as pulse regulators and vasodilators
INVENTOR(S): Sekiya, Tetsuo; Tsutsui, Mikio; Kikuchi, Junko; Horii, Daijiro; Ishibashi, Akira; Suzuki, Junko
PATENT ASSIGNEE(S): Mitsubishi Kasei Corp., Japan

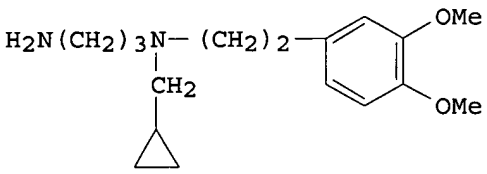
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02138161	A2	19900528	JP 1988-293112	19881119

PRIORITY APPLN. INFO.: JP 1988-293112 19881119
OTHER SOURCE(S): MARPAT 113:190946
GI



I



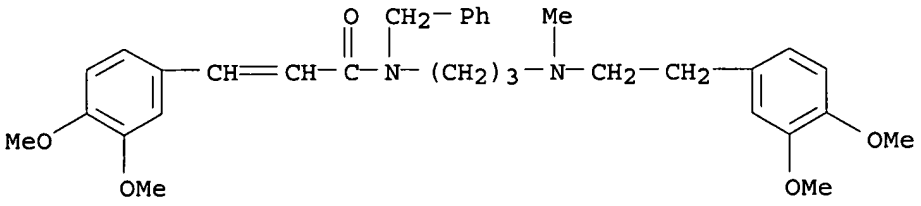
II

AB Cinnamamide derivs. [I; X, Y = H, halo, CF3, C2-5 alkyl, alkoxy; Z = (substituted) C2-4 alkylene; R1 = H, C2-8 alkyl, PhCH2, R1NZ = heterocyclyl; R2 = C1-8 alkyl, PhCH2; m, n, q = 1-3] and their **pharmaceutically** acceptable salts are prepd. ClCO2Et was added to a soln. of cinnamic acid and Et3N in CH2Cl2 under cooling and the mixt. stirred at room temp., amine II was added with stirring to give 54% I [X = H, Yq = 3,4-(MeO)2, R2 = H, R2 = cyclopropylmethyl, m = 2, Z = (CH2)3]. Also prepd. were 45 addnl. I. I showed heartbeat regulatory activity at 3.0 .mu.M and 53.9% vasodilating activity at 10 .mu.M.

IT **129989-57-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as heartbeat regulator and vasodilator)

RN 129989-57-7 CA

CN 2-Propenamide, 3-(3,4-dimethoxyphenyl)-N-[3-[[2-(3,4-dimethoxyphenyl)ethyl]methylamino]propyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

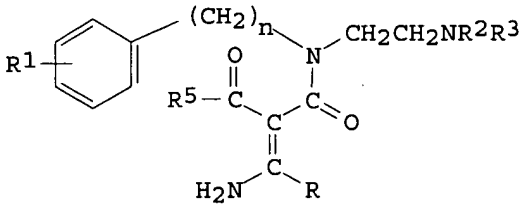


IT **129989-57-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as heartbeat regulator and vasodilator)

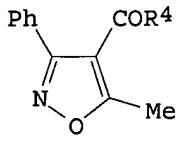
L15 ANSWER 60 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 108:150066 CA
TITLE: Preparation of N,N-disubstituted alkenamides and phenylalkenamides as antidiabetic agents
INVENTOR(S): Nadelson, Jeffrey
PATENT ASSIGNEE(S): Sandoz Pharmaceuticals Corp., USA
SOURCE: U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 505,804, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4681898	A	19870721	US 1984-608126	19840508
PRIORITY APPLN. INFO.:			US 1981-330601	19811214
			US 1983-505804	19830620

OTHER SOURCE(S): CASREACT 108:150066
GI



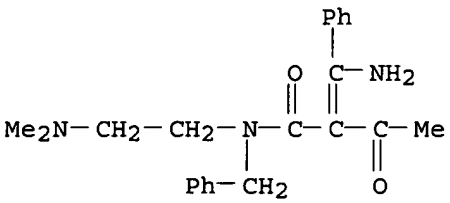
I



II

AB The title amides [I; R = alkyl, Ph, R1C6H4; R1 = H, halo, alkyl, alkoxy; R2, R3 = alkyl; R2R3 = (CH2)4-6; R2R3N = morpholino; R5 = H, C1-6 alkyl; n = 0, 1] and their **pharmaceutically** acceptable salts, useful as antidiabetics and hypoglycemics, are prepd. A soln. of phenylisoxazole deriv. II (R4 = Cl) in THF was added to a mixt. of Me2NCH2CH2NHPh and Et3N in THF under cooling and stirred at room temp. to give amide II (R4 = Me2NCH2CH2NPh), which was hydrogenated over 10% Pd-C at 50-60.degree. and 50 psi H to give I (R = Ph, R1 = H, R2 = R3 = R5 = Me, n =0), which (350 mg) was formulated with 150 mg lactose to give a capsule showing ED25 of 74 mg/kg p.o. in treating diabetes in mammals, vs. 110 mg/kg with tolbutamide.

IT **88098-99-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as hypoglycemic agent)
RN 88098-99-1 CA
CN Butanamide, 2-(aminophenylmethylene)-N-[2-(dimethylamino)ethyl]-3-oxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

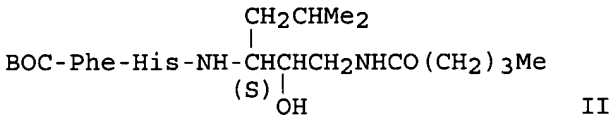


IT **88098-99-1P 88099-04-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as hypoglycemic agent)

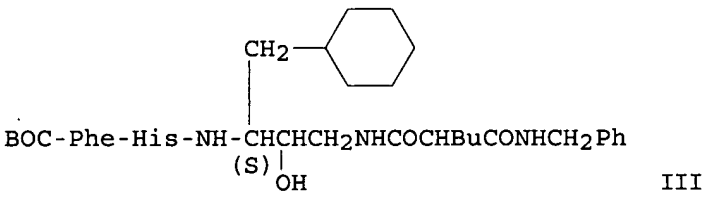
L15 ANSWER 61 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 108:75856 CA
TITLE: Preparation of peptides as renin inhibitors
INVENTOR(S): Gordon, Eric Michael
PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc. , USA
SOURCE: Eur. Pat. Appl., 69 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 223437	A2	19870527	EP 1986-308270	19861023
EP 223437	A3	19890830		
R: DE, FR, GB, IT				
US 4749781	A	19880607	US 1986-909434	19860919
CA 1282549	A1	19910402	CA 1986-520676	19861016
JP 62126158	A2	19870608	JP 1986-269514	19861112

PRIORITY APPLN. INFO.: US 1985-797321 19851112
OTHER SOURCE(S): CASREACT 108:75856
GI



II



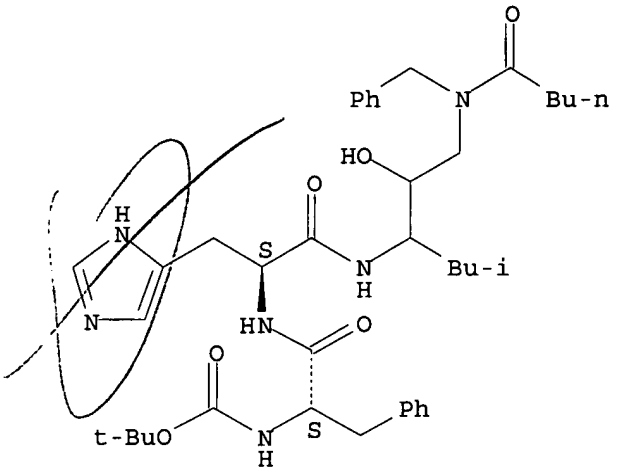
III

AB X-NHCHR4CONHCHR3CH(OH)CH2NR2COCHR1R5 (I; X = substituted .alpha.-aminoalkanoyl; R1, R2 = H, alkyl, .omega.-arylalkyl, .omega.-cycloalkylalkyl, .omega.-heterocycycylalkyl; R3, R4 = H, haloalkyl, .omega.-carbamoylalkyl, etc.; R5 = H, alkyl, .omega.-cycloalkylalkyl, .omega.-arylalkyl, .omega.-heterocycylalkyl, etc.] and their **pharmaceutically** acceptable salts, useful as renin inhibitors and therefore in the treatment of hypertension (no data), are prepd. Peptide II was prepd. in many steps from (S)-Me2CHCH2CH(COCH2Cl)NHCO2CMe3 via hydride redn., dehydrochlorination, N-acylation with valeryl chloride, etc. Tablets were prepd. each contg. peptide III 250, cornstarch 100, gelatin 20, Avicel 50, and Mg stearate 5 mg.

IT **112739-52-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of, as antihypertensive)
RN 112739-52-3 CA
CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[1-[1-hydroxy-2-[(1-oxopentyl)(phenylmethyl)amino]ethyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



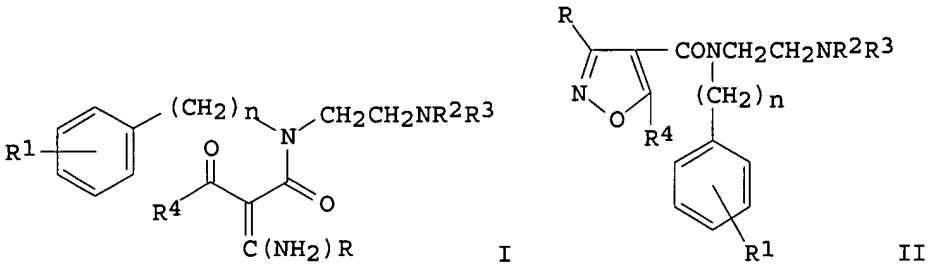
IT **112739-52-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antihypertensive)
IT **112739-71-6P 112739-72-7P 112762-74-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for antihypertensive peptides)

L15 ANSWER 62 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 100:6099 CA
TITLE: N,N-Disubstituted alkenamides and phenylalkenamides and their use as **pharmaceuticals**
INVENTOR(S): Nadelson, Jeffrey
PATENT ASSIGNEE(S): Sandoz A.-G., Switz.; Sandoz-Patent-G.m.b.H.; Sandoz-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 84292	A1	19830727	EP 1982-810533	19821209
EP 84292	B1	19850213		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 11770	E	19850215	AT 1982-810533	19821209
DK 8205534	A	19830615	DK 1982-5534	19821213
JP 58110549	A2	19830701	JP 1982-219144	19821213
HU 27472	O	19831028	HU 1982-4019	19821213
HU 189626	B	19860728		

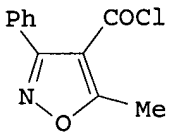
CA 1191511	A1	19850806	CA 1982-417542	19821213
IL 67464	A1	19860831	IL 1982-67464	19821213
FI 8204298	A	19830615	FI 1982-4298	19821214
AU 8291476	A1	19830623	AU 1982-91476	19821214
AU 561008	B2	19870430		
ES 518186	A1	19840601	ES 1982-518186	19821214
ZA 8209190	A	19840725	ZA 1982-9190	19821214
PRIORITY APPLN. INFO.:			US 1981-330601	19811214
			EP 1982-810533	19821209

GI



I

II



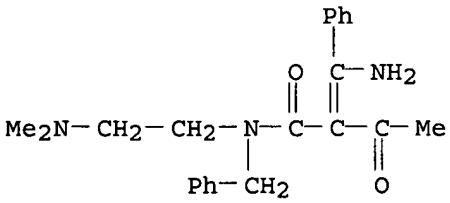
III

AB Title amides I [R = C1-4 alkyl, substituted Ph; R1 = halo, C1-4 alkyl, C1-4 alkoxy; R2, R3 = C1-4 alkyl; R2R3 = (CH2)m (m = 4, 5, 6), CH2CH2OCH2CH2; R4 = H, C1-6 alkyl; n = 0, 1], useful as antidiabetics (no data), were prepd. by the reductive cleavage of isoxazoles II. Thus, PhNHCH2CH2NMe2 was acylated with acid chloride III in THF contg. Et3N to give II (R = Ph, R1 = H, R2-R4 = Me, n = 0), which was cleaved by hydrogenolysis over Pd/C to give I (R = Ph, R1 = H, R2-R3 = Me, n = 0).

IT **88098-99-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 88098-99-1 CA

CN Butanamide, 2-(aminophenylmethylene)-N-[2-(dimethylamino)ethyl]-3-oxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT **88098-99-1P 88099-04-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L15 ANSWER 63 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 86:71947 CA
TITLE: **Pharmaceutically** useful carboxylic acid

amides
INVENTOR(S): Linke, Siegfried; Sitt, Ruediger
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 109 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

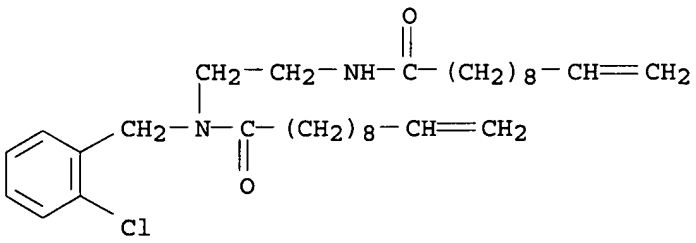
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2515146	A1	19761021	DE 1975-2515146	19750408
SE 7602707	A	19761009	SE 1976-2707	19760227
NO 7601050	A	19761011	NO 1976-1050	19760325
FI 7600919	A	19761009	FI 1976-919	19760406
NL 7603594	A	19761012	NL 1976-3594	19760406
BE 840469	A1	19761007	BE 1976-165915	19760407
DK 7601641	A	19761009	DK 1976-1641	19760407
JP 51127002	A2	19761105	JP 1976-38348	19760407
ZA 7602088	A	19770427	ZA 1976-2088	19760407
FR 2306683	A1	19761105	FR 1976-10309	19760408

PRIORITY APPLN. INFO.: DE 1975-2515146 19750408
DE 1975-2551483 19751117

AB A total of 168 amides, most of them aliph. diamides, are prepd. by acylation of polyamines with acid chlorides or acids and ClCO2Et. Lipid-lowering data are given for .apprx.50 amides. Thus, reaction of H2N(CH2)3NH2 with CH2:CH(CH2)8COCl in THF in presence of Et3N at 5.degree. and 2 hr stirring at 60.degree. gives 84% CH2:CH(CH2)8CONH(CH2)3NHCO(CH2)8CH:CH2.

IT **61797-03-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antilipemic activity of)

RN 61797-03-3 CA
CN 10-Undecenamide, N-[(2-chlorophenyl)methyl]-N-[2-[(1-oxo-10-undecenyl)amino]ethyl]- (9CI) (CA INDEX NAME)



IT **61797-03-3P 61797-12-4P 61797-13-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antilipemic activity of)

L15 ANSWER 64 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 63:34608 CA
ORIGINAL REFERENCE NO.: 63:6210h,6211a-b
TITLE: Easily obtainable antiserotonin which has little effect on the brain
AUTHOR(S): Dombro, R. S.; van der Hoeven, T.; Woolley, D. W.
CORPORATE SOURCE: Rockefeller Inst., New York, NY
SOURCE: Nature (1965), 206(4984), 631-2

DOCUMENT TYPE: Journal
LANGUAGE: English

AB m-Methoxy-N-benzylcinnamamide was mixed with 2 equivs. of NaH in HCONMe2 or Me2SO, treated with 1.1 equivs. of ClCH2CH2NH2.HCl in the same solvent and allowed to react 20 hrs. (120.degree. with HCOMe2, room temp. with Me2SO), the mixt. dild. with EtOAc, and extd. with aq. HCl. The mixt. was made alk. and extd. with EtOAc, the ext. concd., and the bioxalate formed by addn. of (CO2H)2 to an Me2CO soln. of the residue, to give N-aminoethyl-N-benzyl-m-methoxycinnamamide bioxalate, m. 188-90.degree.; hydrochloride, m. 191-3.degree.. This compd. will not readily pass through the blood-brain barrier and is useful to test peripheral actions. In the rat uterus test, the hydrochloride gave half-max. inhibition at 0.4 .gamma./ml. against 0.01 serotonin/ml. This was 15% as effective as the corresponding dimethylamino compd. (III) (CA, 60, 16361a). The **drug** gave a median effective dose of 30 mg./kg. against diarrhea from administered 5-hydroxytryptophan in mice. Thus, in the diarrhea test, the compd. is more potent than III but less potent than hydrazinodole.

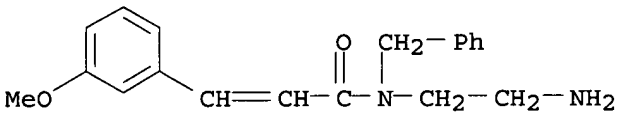
IT **3115-15-9**, Cinnamamide, N-(2-aminoethyl)-N-benzyl-m-methoxy-, oxalate (1:1)
(prepn. of)

RN 3115-15-9 CA

CN Cinnamamide, N-(2-aminoethyl)-N-benzyl-m-methoxy-, oxalate (1:1) (8CI) (CA INDEX NAME)

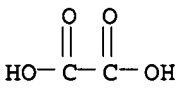
CM 1

CRN 554-39-2
CMF C19 H22 N2 O2



CM 2

CRN 144-62-7
CMF C2 H2 O4



IT **3115-15-9**, Cinnamamide, N-(2-aminoethyl)-N-benzyl-m-methoxy-, oxalate (1:1)
(prepn. of)

IT **554-39-2**, Cinnamamide, N-(2-aminoethyl)-N-benzyl-m-methoxy-
(serotonin inhibition by, brain and)

IT **3115-16-0**, Cinnamamide, N-benzyl-N-[2-(dimethylamino)ethyl]-m-methoxy-
(serotonin inhibition by, N-(2-aminoethyl)-N-benzyl-m-methoxycinnamamide and)

L15 ANSWER 65 OF 65 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 60:93472 CA
ORIGINAL REFERENCE NO.: 60:16361a-c

10/019,993

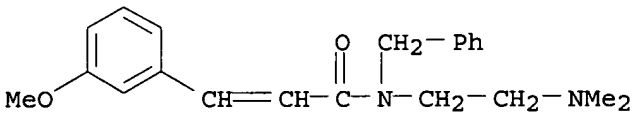
TITLE: Cinnamamides as structural analogs and antagonists of serotonin
AUTHOR(S): Dombro, R. S.; Woolley, D. W.
CORPORATE SOURCE: Rockefeller Inst., New York, NY
SOURCE: Biochem. Pharmacol. (1964), 13(4), 569-76
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Cinnamamides with aminoalkyl groups on the amide nitrogen were conceived as structural analogs of serotonin which would act as antimetabolites of it. Several such amides were synthesized and tested for antiserotonin activity on the isolated rat uterus and in living animal. All such amides that were tested acted as antagonists of the hormone. When the structural analogy to serotonin was increased by introduction of a meta-methoxyl group in the benzene ring, antiserotonin potency was increased considerably. A further increase in potency was achieved by introduction of a benzyl group on the amide nitrogen. The most active cinnamamide proved to be more active as a serotonin antagonist in the rat uterus assay than the previously known and highly potent 1-benzyl-2-methyl-5-methoxytryptamine (BAS), and was much easier to synthesize. It was, however, less active than BAS in the in vivo assay that was used. The compounds were not antagonistic toward acetylcholine or bradykinin on rat uterus. It was suggested that some previously known cinnamamides may owe some of their **pharmacol**. activity (e.g. local anesthetic) to their ability to act as antimetabolites of serotonin.

IT **10231-08-0**, Cinnamamide, N-benzyl-N-[2-(dimethylamino)ethyl]-m-methoxy-, hydrochloride
(prepn. and serotonin antagonism by)

RN 10231-08-0 CA

CN 2-Propenamide, N-[2-(dimethylamino)ethyl]-3-(3-methoxyphenyl)-N-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

IT **10231-08-0**, Cinnamamide, N-benzyl-N-[2-(dimethylamino)ethyl]-m-methoxy-, hydrochloride **106458-10-0**, Cinnamamide, N-benzyl-N-[2-(dimethylamino)ethyl]-o-methoxy-, hydrochloride **106630-90-4**, Cinnamamide, N-benzyl-N-[2-(dimethylamino)ethyl]-p-methoxy-, hydrochloride
(prepn. and serotonin antagonism by)

=> d his

(FILE 'HOME' ENTERED AT 14:36:28 ON 29 JAN 2003)

FILE 'REGISTRY' ENTERED AT 14:36:34 ON 29 JAN 2003

L1		STRUCTURE UPLOADED
L2	10	S L1 SAM
L3	970	S L1 FULL
L4	683	S L3 AND CA/LC
L5	287	S L3 NOT L4
L6	0	S L5 AND USPATFULL/LC

```
L7            12 S L5 AND CAOLD/LC
L8           275 S L5 NOT L7
L9            10 S L8 AND CAPLUS/LC
L10          265 S L8 NOT L9

     FILE 'CA' ENTERED AT 14:41:23 ON 29 JAN 2003
L11          253 S L3
L12        75029 S CNS OR (CENTRAL NERVOUS)
L13            7 S L12 AND L11
L14          246 S L11 NOT L13
L15           65 S L14 AND (PHARM? OR DRUG)

=
=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

STN INTERNATIONAL LOGOFF AT 14:45:01 ON 29 JAN 2003
```